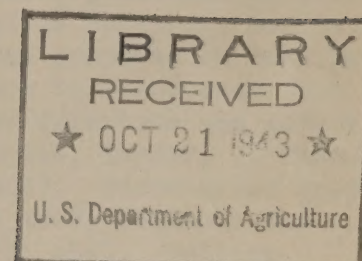


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UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH ADMINISTRATION
BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY



REFERENCES ON THE PREPARATION,
PROPERTIES, AND USES OF LACTIC ACID
AND ITS DERIVATIVES

Compiled in the Carbohydrate Division,
Eastern Regional Research Laboratory,
Chestnut Hill Station,
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A. PREPARATION AND PROPERTIES OF METHYL LACTATE

1. Methyl lactate was prepared, apparently for the first time, by L. Schreiner (Ann. 197, 1-26(1879)) by heating lactic acid and methanol in a sealed tube at 160° C. (Beilstein III, 280). The following constants were given: $b_{760} 144.8^{\circ}$ (corrected); d_0 1.1180; d_{19} 1.0898; d_{80} 1.0280; d_{90} 1.0176. The temperature of 150° was not found satisfactory for making methyl and ethyl lactates, but a good yield was claimed for 160° . The ester forms an addition compound with calcium chloride.
2. B. Prager and P. Jacobson, Beilstein's Handbuch der Organischen Chemie, Vierte Auflage (review of literature to 1910), Julius Springer, Berlin, 1921, Vol. III, pp. 264, 280. Methyl d-lactate was prepared by heating d-lactic acid and methanol and allowing the mixture to stand over lime (Le Bel, Bull. soc. chim.(3) 9, 678). From silver d-lactate and methyl iodide (Walker, J. Chem. Soc. 67, 916; compare Purdie, Lander, J. Chem. Soc. 73, 296; Purdie, Irvine, J. Chem. Soc. 75, 484). Recommended preparation: From the zinc ammonium salt of d-lactic acid, methanol and sulfuric acid (Purdie and Irvine, J. Chem. Soc. 75, 484). Boiling points: 58° at 19 mm.; $60-1^{\circ}$ at 35 mm.; density 1.0895 at 20° , 1.0335 at 70° ; rotation between 10° and 70° (Walker, Chem. Zentralblatt 1909, II, 2118).

Treatment of methyl d-lactate with methyl iodide and silver oxide yielded methyl methoxypropionate (Purdie, Irvine, J. Chem. Soc. 75, 485)

Methyl dl-lactate.--From heating lactic acid and methanol in a sealed tube at 160° ; boiling point at 760 mm., 144.8° (corrected); density 1.1180 at 0° , 1.0898 at 19° , 1.0280 at 80° , 1.0176 at 90° ; hydrolyzed with water; formed addition complex with calcium chloride (Schreiner, Ann. 197, 12). Detection with color test (Takahashi, Chem. Zentralblatt 1907, II, 1660).

Treatment of methyl lactate with 2 vol. sulfuric acid (d 1.84) and 1 vol. nitric acid (d 1.4) at 0° yielded the nitrate; boiling point $85-7^{\circ}$ at 35 mm., density 1.2488 at 7° C. (de Varda, Gazz. chim. Ital. 21, II, 359).

3. F. Richter, Beilsteins Handbuch der Organischen Chemie, Vierte Auflage, Erstes Ergänzungswerk (literature 1910-19), Julius Springer, 1929, Vols. III & IV, pp.101. Methyl l-lactate boils at 40° (13 mm.), 48° (16 mm.); these and other physical constants are given by Patterson and Forsyth (J. Chem. Soc. 103, 2266). Density 1.097 at 15° and 1.093 at 20° ; these and other physical properties are given by Clough (J. Chem. Soc. 113, 552).

Methyl l-lactate and acetic anhydride give methyl l-acetoxypropionate; boiling point $171-2^{\circ}$; $68-70^{\circ}$ at 13 mm.; density 1.0885 at 19.8° ; these and other data are reported by Patterson and Forsyth.

Methyl dl-lactate.--Rates of hydrolysis (hydrochloric acid and sodium hydroxide) were determined by Palomaa (Chem. Zentralblatt 1913, II, 1956, 1918, I, 1143).

4. W. J. Bannister (to Commercial Solvents Corp.) Aliphatic esters of Carboxylic Acids: U. S. 2,029,694, Feb. 4, 1936; CA 30, 1807 (1936); cf. CA 29, 6902. Methyl, ethyl and butyl lactates are prepared from the alcohols and lactic acid by introducing the alcohol into the acid at temperatures ranging from the boiling point of the formed ester to approximately 20° below said boiling point and removing the resulting vapors of the formed ester, water and excess alcohol.
- 4a. B. T. Brooks, (to Standard Alcohol Co.) Hydroxy Aliphatic Esters: U.S. 2,176,201, Oct. 17, 1939; CA 34, 1033(1940). Reaction is effected between methyl formate or of a hydroxy lower molecular weight saturated fatty acid and an aliphatic alcohol containing not more than 5 carbon atoms (suitably MeOH at 100-140° under pressure).
5. O. Burkard and L. Kahovec, Raman Effect. LXXXII. Nitrogen Compounds. 10. (alpha-Amino and alpha-hydroxy-propionic Acids and their Esters; Monatsh. 71, 333-45 (1938); C.A. 32, 8270(1938). Raman spectra of lactic acid and its methyl, ethyl, isopropyl and butyl esters are recorded. Raman spectra for the corresponding alpha-methoxypropionates are included. Methyl lactate b 143.3-144.3 at 760 mm. n_D^{19} - 1.4149.

Isopropyl lactate (b.p. 158.6° to 161° at 760 mm) was prepared by heating lactyllactic acid ("Lactylmilchsaure") and isopropyl alcohol at 160-170° in a sealed tube for 4 hours.
6. R. Burns, D. T. Jones, and P. D. Ritchie, Studies in Pyrolysis. I. The Pyrolysis of Derivatives of Acetoxypropionic Acid, and Related Substances: J. Chem. Soc. 1935, 400-6. By treatment of methyl lactate with acetic anhydride and a small amount of concentrated sulfuric acid, methyl acetoxypropionate was obtained in 79-82% yields. By treatment of intermediate fractions with brine, an additional 13% was isolated. B.p. 171.5-172° at 760 mm. and 76-7° at 12 mm.; n_D^{20} 1.4111, and d_4^{20} 1.088. Pyrolysis of methyl acetoxypropionate yielded methyl acrylate.
7. Chemische Fabrik auf Actien, Lactic acid esters: Brit. 256,587, Aug. 7, 1925; C.A. 21, 2906 (1927). A lactic acid salt such as calcium or magnesium lactate is treated with an alcohol (methanol or ethanol) in the presence of an acid such as sulfuric at a temperature below the boiling point of the alcohol used.
8. H. V. Claborn and L. T. Smith. The Acetylation of Lactic Esters by Ketene: J. Am. Chem. Soc. 61, 2727-8 (1939). Ketene reacted with methyl lactate containing a trace of sulfuric acid and gave a 96.4% yield of methyl acetoxypropionate. Following the general method of Burns, Jones and Ritchie (J. Chem. Soc. 1935, 400-6) acetic anhydride was used

to obtain the acetoxypionate in 92% yield.

9. G. W. Clough, The Relationship between the Optical Rotatory Powers and the Relative Configurations of Optically Active Compounds. The Influence of Certain Inorganic Haloids on the Optical Rotatory Powers of alpha-Hydroxy Acids, Amino Acids, and their Derivatives: J. Chem. Soc. 113, 526-554 (1918).--The aqueous lactic acid was obtained by boiling methyl l-lactate with 10 times its weight of water for 6 hours, and subsequent distillation of the methanol.

Most of the paper is devoted to discussion of optical rotation, Walden inversion, etc.

10. G. W. Clough, The Relationship between the Optical Rotatory Powers and the Relative Configurations of Optically Active Compounds; J. Chem. Soc. 127, 2808-13(1925). The optical activity, but not preparative methods of l-lactic acid, methyl l-lactate, and l-lactamide was discussed.
11. G. W. Clough, Relationship between the optical rotatory powers and the relative configurations of optically active compounds. III. J. Chem. Soc. 1926, 1674-6; CA 20, 3279(1926). Optical constants, but no preparative data, are given for methyl d-lactate.
12. I. G. Farb. A.-G., Esters of Lactic Acid: Ger.544,499, Sept. 25, 1925; CA26, 2467(1932).--Lactonitrile is treated in the presence of HCl with an alcohol containing less than five carbon atoms, and the product is treated with water in the presence of an organic solvent in which NH_4Cl is insoluble, e.g., benzene.
13. I. G. Farb. A.-G., Lactic Acid Derivatives: Brit. 290,464, July 2, 1927; CA 23, 849 (1929). A dried neutralized mash in which lactic acid has been produced by fermentation is extracted with methanol which dissolves the lactate. The latter may be separated by distillation of the methanol or by precipitation with acetone or methyl formate. The free acid may be obtained by treating the lactate with inorganic acid or methyl lactate may be produced by adding sulfuric acid to the methanol solution of lactate and other esters of lactic acid may be similarly formed from different alcohols.
14. E. Fischer and H. O. L. Fischer, Carbomethoxy Derivatives of Glycolic Acid and Lactic Acid: Ber. 47, 768-780; C.A. 8, 1769(1914); cf. C.A. 8, 99. Carbomethoxy-lactic acid was prepared in 40% yield from the acid and methyl chloroformate. The chloride was obtained from the acid in 85% yield. The acid chloride of carbomethoxyglycolic acid reacted with benzene in the presence of a catalyst to give a 78.5% yield of carbomethoxybenzoyl carbinol. The analogous reaction with lactic acid derivatives, which should have given a lactophenone derivative, apparently was not tried.

15. K. Freudenberg, F. Brauns, and H. Siegel, Die Konfiguration der Mandelsäure and anderer Oxysäuren: Ber. 56, 193-200(1923). A mixture of 4 g. d-lactic acid and 80 cc. methanol (containing 1% HCl) was refluxed for 4 hours. Most of the solvent was then removed at 20 mm. pressure (35°). The residue was neutralized with potassium carbonate, extracted with much ether, and distilled at 25 mm.; yield 2.5 g.
16. K. Freudenberg, W. Kuhn, and I. Bumann, The Configuration of the Halopropionic Acids and the Alanines: Ber. 63B, 2380-90(1930); CA 25, 492 (1931).

Rotations of the methyl esters, chlorides, and dimethyl-amides of alpha azido, chloro, bromo, and iodopropionic acids, and of benzoyl, acetyl and toluene-sulfonyl lactic acids are tabulated.

Methyl toluenesulfonyllactate, and n-dimethyl-lactamide (60% yield) were prepared.

Directions for making acetylalanine methyl ester were given.

17. K. Freudenberg and L. Markert, Steric Series. VIII. The configuration of alpha-Bromopropionic Acid: Ber. 60B, 2447-2458(1927) CA 22, 943 (1928); cf. CA 20, 1056. Rotations given of following active compounds:

derivatives of chloropropionic acid; methoxypropionic acid, chloride, methyl and propyl esters, amide and dimethylamide; acetoxypropionic acid, chloride, methyl, ethyl and propyl esters, amide and dimethylamide; benzoyloxypropionic acid chloride, methyl ester, dimethyl-amide, and diethylamide; toluenesulfonyllactic acid chloride, amide, dimethylamide and diethylamide.

Ethyl d-lactate was prepared by the method of Wood, Such and Scarf (J. Chem. Soc. 123, 606 (1923) from zinc ammonium lactate, alcohol and H₂SO₄.

Methoxypropionic acid (45% yield) was prepared from potassium lactate and methyl sulfate.

Acetoxypropionic acid was prepared in 84% yield by the method of Anschutz (Ber. 37, 3972(1904)).

Benzoyloxypropionyl chloride was prepared by the method of B. Helferich and L. Keiner (Ber. 57, 1618 (1924)).

18. K. Freudenberg and F. Rhino, Die Konfiguration des Alanins: Ber. 57, 1547-1557 (1924).

Using a method previously described (E. Fischer and A. Speier, Ber. 28, 3255 (1895); K. Freudenberg and F. Rhino, Ber. 56, 199 (1923)), methyl and ethyl lactates were prepared in approx. 60% yield. The following

were prepared: ethyl d-acetoxypropionate (80% yield); ethyl hexahydrobenzoyloxypropionate; methyl benzoyloxypropionate (70%); benzoyloxypropionamide; methyl toluenesulfonyllactate; ethyl toluenesulfonyllactate; toluenesulfonyllactate (65% yield); and corresponding derivatives of alanine.

19. E. Fischer and A. Speier, Darstellung der Ester: Ber. 28, 3252-8(1895). The preparation of ethyl and, occasionally, methyl esters of many acids was studied. Some of the results are given below:

: :	: :	: :	:Heating: :period,:	Yield :	:
: Acid, g.	:Alcohol, g.	:acid, g.	: hrs.	: g.	: %
:Benzoic, 50	:Ethyl, 100	:HCl, 3	: 2	:46.8	: 76
:Benzoic, 50	:Ethyl, 100	:H ₂ SO ₄ , 10	: 3	:55	: 90
:Cinnamic, 15	:Ethyl, 45	:HCl, 1.35	: 5	:15.4	: 86.3
:Cinnamic, 15	:Ethyl, 45	:H ₂ SO ₄ , 4.5	: 5	:16	: 89.7
:Mandelic, 5	:Ethyl, 15	:HCl, 0.15	: 4	: 4	: 67.5
:Mandelic, 5	:Ethyl, 15	:H ₂ SO ₄ , 1.5	: 4	: 3.7	: 62.5
:Glycolic, 10	:Ethyl, 30	:HCl, 0.3	: 4	: 9	: 65.8
:Malic, 10	:Ethyl, 40	:HCl, 0.4	: 4	:10	: 70.5
:Tartaric, 20	:Ethyl, 80	:HCl, 0.8	: 4	:20	: 72.8
:Mucic, 5	:Ethyl, 25	:HCl, 0.75	: 12	: 3	: 47.3
:Mucic, 5	:Methyl, 25	:HCl, 0.75	:24 at	: 5.15	: 90.8
:	:	:	: 100°	:	:

20. G. Genin, The Manufacture of Pure Lactic Acid: Lait 20, No.197, 412-17 (1940); CA 35, 6927(1941). Preparation of Pure lactic acid through the production and hydrolysis of methyl lactate was recommended.
21. J. W. E. Glattfeld and D. Macmillan, Lactones in Liquid Ammonia: J. Am. Chem. Soc. 58, 898-901 (1936). Methyl, ethyl, propyl and butyl lactates were ammonolyzed by liquid ammonia.
22. H. Gorgeot, Lactic Acid Esters: Fr. 678,627, Nov. 12, 1928, CA 24, 3516 (1930). The dry alkaline earth lactate is treated with alcohols in the presence of mineral acid just sufficient to liberate the lactic acid.
23. Frank Hartwich, to Schering-Kahlbaum A.-G., Lactic Acid Esters: Ger. 518,388, Jan. 23, 1926. CA 25, 2437(1931).

A mixture of magnesium lactate, an alcohol, and an acid, with or without a catalyst, e.g., an excess of acid or calcium chloride, is heated.

(Alcohol not mentioned in CA)

24. Le Bel, Bull. Soc. chim. 37 9 678. d-Methyl lactate was prepared by heating d-lactic acid with methanol, followed by standing over lime.
25. M. H. Palomaa, Influence of the Position of the Oxygen Atom in the Chain on the Velocity of Ester Hydrolysis: Ann. Acad. Sci. Fennicae (A) 4, 1-104; Chem. Zentr. 1913, II, 1956; C.A. 8, 1772 (1914). The following lactic acid derivatives were studied: methyl lactate, ethyl lactate, methyl methoxypropionate, and ethyl ethoxypropionate.
26. T. S. Patterson and W. C. Forsyth, The Influence of Solvents on the Rotation of Optically Active Compounds, XIX, The Rotation of certain Derivatives of Lactic Acid: J. Chem. Soc. 103, 2263-71 (1913).--Methyl d-lactate was observed to be readily volatile with methanol, i.e., the methanol fraction had slight optical activity. Sp. gr. = 1.2042 (-75); 1.1882 (-62); 1.1752 (-51); 1.1205 (-8.6); 1.0971 (16.7); 1.0960 (17.8); 1.0751 (35.4); 1.0518 (56); 1.0256 (78.8) 1.0048 (96.7); .9725 (125). Methyl acetoxypionate was made by boiling methyl l-lactate with excess acetyl chloride; b_{13} 68-70 and 171-2° at atmospheric pressure.
27. T. S. Patterson and A. Lawson, Influence of Solvents and other Factors on the Rotation and the Rotation--Dispersion of Optically Active Compounds. XXVII. Derivatives of Lactic Acid: J. Chem. Soc. 1929, 2042-51; CA 24, 63(1930); cf. CA 23 820. Following are prepared: methyl lactate, methyl acetoxypionate, methyl dichloroacetoxypionate, methyl trichloro-acetoxypionate, methyl methoxypionate, methyl benzoyloxypionate, methyl o-nitrobenzoyloxypionate, methyl m-nitrobenzoyloxypionate, and methyl chlorosulfinylpropionate, and chloroacetoxypionate. Prepared Me lactate by method of Purdie & Irvine, J. C. S. 75, 484(1899) and Patterson, Forsyth, B.p. = 47° at 15 mm. Densities given at various temperatures.
- The preparation of zinc ammonium lactate was described in detail.
- Methyl l-lactate was prepared by the method of Purdie and Irvine (J. Chem. Soc. 75, 484(1899) and Patterson and Forsyth (J. Chem. Soc. 103, 2263(1913)), the zinc ammonium lactate having been carefully dried until 2 moles of water were removed. Yield obtained by Patterson and Lawson was not given.
28. I. Peyches, The Raman spectra of some acids and alcohols and their Derivatives; esters and salts: Bull. soc. chim. (5) 2, 2195-2209(1935) CA 30, 2492(1936) cf. CA 29, 682. The Raman spectra of lactic and glycolic acids and their esters and salts were compared with acetic and propionic acids, esters, and salts. (Specific lactic esters not mentioned in Chem. Abstracts).

29. E. J. Powers (to Commercial Solvents Corp.), Acylated Esters of Hydroxy Acids: Can. 310,854, Apr. 28, 1931. CA 25, 3015(1931). A mixture of a hydroxy aliphatic acid and ester is refluxed in the presence of catalyst, e.g., HCl, H₂SO₄, H₃PO₄, etc.
- 29a. T. Purdie and J. C. Irvine, The Rotatory Powers of Optically Active Methoxy and Ethoxy Propionic Acids prepared from Active Lactic Acid: J. Chem. Soc. 75, 483-493(1899).--Methyl d-lactate was prepared (37 g. yield) from 120 g. zinc ammonium d-lactate, 462 g. methanol, and 96 g. sulfuric acid. $B_{19}^{58^\circ}$; d_4^{20} 1.0925. The yield by this process was so small that silver salt method was preferred. From 91 g. silver salt and 136g. methyl iodide was obtained 37 g. of ester, boiling at 58-62° under 22-33 mm. pressure. Ethyl d-lactate was prepared similarly in comparable yield.

Silver oxide (1.5 moles) was added gradually to a mixture of 1 mole methyl lactate and 3 moles methyl iodide. Yield of crude ester was 65%.

30. T. Purdie and G. D. Lander, Optically Active Alkyloxypropionic Acids: J. Chem. Soc. 73, 862-878(1898). Using Schreiner's method (Ann. 197, 13 (1897)), 240 g. (approx. 50%) ethyl ethoxypropionate was obtained from 580 g. ethyl bromopropionate. The cause of the low yield was attributed to the formation of ethyl acrylate.

Methyl methoxypropionate (186 g. or 53% yield) was made from methyl bromopropionate (500 g.).

Propyl bromopropionate (200 g.) was added gradually to a hot solution of 26g. sodium in 400 g. propyl alcohol. Heated for 1 hr., and then treated with CO₂. Yield was 55%; b.p. 137-8°.

31. P. D. Ritchie, Studies in Pyrolysis. III. The Pyrolysis of carbonic and Sulfurous Esters: J. Chem. Soc. 1935, 1054-61. Carbonyl chloride was blown into a vigorously stirred mixture of 208 g. (2 moles) methyl lactate and 160 g. pyridine until 140 g. had been absorbed. After heating at 100° for 2 hours, isolation procedures were used to obtain 20% methyl chloropropionate, 40% of the carbonate, and 32 g. of liquid boiling at 110° (22 mm.). Pyrolysis of the carbonate yielded methyl acrylate. Methyl lactate and methyl chloroformate gave 73% yield methyl carbomethoxyethyl carbonate; pyrolysis yielded methyl acrylate.
32. P. D. Ritchie, D. T. Jones, and R. Burns, Improvements in or relating to the manufacture of derivatives of unsaturated acids: Brit. 424,885, Mar. 4, 1935. Methyl lactate (208 g.) and 160 g. pyridine and treated with 210 g. methyl chloroformate and heated at 100°C. The product boiled at 198 - 200° at 759 mm., 97-98° at 18 mm., 91.5-2° at 12 mm. Pyrolysis yielded methyl acrylate.

Pyrolysis of methyl alpha-acetoxypromionate yielded methyl acrylate.

The carbonate of methyl lactate (6.172 at 32 mm) was prepared.

33. P. D. Ritchie, D. T. Jones and R. Burns, Manufacture of Derivatives of Unsaturated Acids: U.S. 2,265,814, Dec. 9, 1941.

Some of the esters prepared and pyrolyzed are: acetoxypionitrile, methyl acetoxypionate, ethyl acetoxypionate, di-(alpha-carboethoxyethyl) sulfite, di-(alpha-carbomethoxyethyl) carbonate, and methyl carbomethoxyethyl carbonate. Pyrolysis of these compounds yielded acrylic esters or acrylonitrile.

34. E. J. Salmi, The Influence of Chain Length of the Acyl Component of the Ester upon the Velocity of Acid Hydrolysis of Aliphatic Carboxylic Acid Esters; Ann. Acad. Sci. Fennicae A48, No. 4, 17 pp.(1937);CA33, 8173 (1939). Constants for the velocity of hydrolysis (catalysis by 0.2080 N HCl) of methyl esters of the following acids at 25°C. are: butyric, 0.00423; valeric, 0.00441; glycolic, 0.00716; lactic 0.00780; acrylic, 0.000282.
35. E. J. Salmi and T. Suonpaa, Untersuchungen über atherartig Verbindungen. VII. Zum Einfluss der Chloratom auf die Geschwindigkeit der spontanen wasserverseifung der Ester: BER. 73, 1126-1131, (Oct. 1940). The hydrolysis of several esters, including the ones listed below, was studied:

The Relative K_s Values of esters of hydroxy acids at 25° C.

Acid component	n-alkyl ester	Methylene ester	Ethylidene ester	Trichloroethylidene ester
Glycolic acid	91.8	-	-	169
Lactic acid	100	100	100	100
alpha-Hydroxyisobutyric acid	33.3	33.2	47.1	9.45
Methylethylglycolic acid	10	9.5	24.3	2.93

36. S. Santiago and A. P. West, Chaulmoogryl derivatives of lactates and salicylates: Phillippine J. Sci. 35, 405-9(1928). CA 22, 3638 (1928). The following were prepared by treating the proper ester with chaulmoogryl chloride for 4 days at about 140-180° and crystallizing from methanol with bone black: methyl chaumoogryl lactate (m.p. 51-4°, 38% yield) and ethyl chaumoogryl lactate (m.p. 54-7°, 33% yield).
37. Schering-Kahlbaurn, Lactic Acid Esters, Brit. 319,043, June 14, 1928, CA 24 2470(1930).

An acid such as fulfuric acid is added with cooling to a lactate such as magnesium lactate and an alcohol such as ethanol; after standing the mixture is heated to somewhat below the boiling point of the alcohol, nearly neutralized and is then finally heated to a slightly higher temperature than before (but still below the boiling point of the alcohol), followed by cooling, complete neutralization and isolation of the product.

38. Schering-Kahlbaum A.-G., Lactic Acid Esters: Ger. 518,388, Jan. 23, 1926; CA 25, 2437 (1931). A mixture of magnesium lactate, an alcohol and an acid, with or without a catalyst, e.g., an excess of acid or calcium chloride, is heated.
39. L. Schreiner, Ueber die Siedepunkte der Ester und Aether-Ester der Oxysauren: Ann. 197, 1-26 (1879). Although heating lactic acid and alcohol at 150° was unsatisfactory, the same procedure at 160° gave ethyl lactate and methyl lactate in good yields. Alkoxy esters were prepared from alkyl bromopropionates and sodium alcoholate. Constants given are:

	B.p. °C.:	Density		
		0°C	:	19°C
Methyl lactate	144.8	1.1180	:	1.0898
Ethyl lactate	154.5	1.0546	:	1.0308
Ethyl methoxypropionate	135.5	.9906	:	.9765(18°)
Ethyl ethoxypropionate	155	.9498	:	.9326
	:	:	:	:
				1.0280(80) 1.0176(90)
				.9854(60)
				.9280(66)
				.8862(65)

40. L. T. Smith and H. V. Claborn, Lactic Esters. Preparation and Properties. Ind. Eng. Chem. 32, 692-4(1940). Detailed directions are given for preparing methyl lactate and other esters from calcium, sodium, and zinc lactate in high yields. Sulfuric acid is used to neutralize calcium lactate. The original article should be consulted for details and physical constants of many lactic esters.
41. L. T. Smith and H. V. Claborn, The Production of Pure Lactic Acid: Ind. Eng. Chem., News Ed. 17, 641(1939). The production of high quality lactic acid through methyl lactate is recommended. The preparation of esters and the manufacture, purification, and uses of lactic acid are reviewed.
42. L. T. Smith, C. H. Fisher, E. M. Filachione, W. P. Ratchford, and M. L. Fein, Pyrolysis of Lactic Acid Derivatives. Methyl Lactate, Acetoxypionic Acid, Acetoxypionyl Chloride, and Alkyl Acetoxypionates: Presented before Division of Organic Chemistry, Am. Chem. Soc., Memphis meeting, April 1942.

Thermal decomposition of methyl lactate yielded acetaldehyde, carbon monoxide, and methanol.

43. L. T. Smith, C. H. Fisher, W. P. Ratchford, and M. L. Fein, Pyrolysis of Lactic Acid Derivatives. Conversion of Methyl Acetoxypionate into Methyl Acrylate: Ind. Eng. Chem. 34, 473-479(1942).

Treatment of methyl lactate with 10% excess acetic anhydride (trace of sulfuric acid) yield methyl acetoxypionate (93.5% yield), B.p. 171°; 85° at 31.5 mm. Pyrolysis of the product under various conditions yield

methyl acrylate.

44. M. Takahashi, On the Detection of methyl lactate: Bull. Coll. Agr. Tokyo 7, 565-6; CA 2, 1477(1908). Colorimetric test described.
45. Edward Thorpe, A Dictionary of Applied Chemistry, Vol. IV, 1922, pp.5-11, Longmans, Green and Co. Excellent review of the manufacture, properties, and uses of lactic acid and its salts; the methyl, ethyl, ethylidene, and glyceryl esters are described briefly.
46. V. von Richter, R. Auschutz, and F. Reindel, Organic Chemistry or Chemistry of the Carbon Compounds, Nordemann Publishing Co., N.Y.C., 1934, pp.415-421.

Lactic acid and its methyl and ethyl esters are reviewed briefly. Lactide formation is discussed.

47. C. E. Wood, J. E. Such, and F. Scarf, Rotatory Dispersion of the Esters of Lactic Acid. I. Normal Esters: J. Chem. Soc. 123, 600-16(1923); CA 17, 1952 (1923). The original article should be consulted for the large number of density and rotation values given for the methyl to n-nonyl esters.

"Preliminary investigations showed that a salt of lactic acid was preferable to the free acid for esterification. The best results were obtained by the use of the zinc ammonium compound."

Methyl d-lactate.--Concentrated H_2SO_4 (19.25 g.) was added slowly to 25 g. dry zinc ammonium l-lactate and 100 cc. methanol. The mixture was heated 4 hrs. on a water bath, cooled, neutralized with potassium carbonate, filtered, and the residue extracted with dry ether. After 4 fractionations, 11 g. (55%) was obtained at 32-3° (8 mm.). $D_{25}^{20} = 1.1037$ (10.7°); 1.0857(26); 1.0556(52.4°); 1.0208(82.7); 0.9782(119°).

Ethyl l-lactate.--Mixture of 36 g. zinc ammonium l-lactate, 195 cc. dry ethanol and 27.8 g. concd. H_2SO_4 was refluxed 4 hrs. and treated as in the case of the methyl ester. Yield: 13 g. (72%) boiling at 53° (15 mm.).

Zinc ammonium l-lactate, g.:	: Alcohol, g.:	: H ₂ SO ₄ :	: Heating period, hrs. :	: g. :	Yield : : % :	: B.p. : : °C. :	: Pressure, mm. :
41	: propyl, :	: 28.5 g. :	: - :	: 23 :	: 52 :	: 70-1 :	: 16 :
	: 40 :	: :	: :	: :	: :	: :	: :
32.5	: n-Butyl, :	: 14 cc. :	: 5, water bath :	: 12 :	: 40 :	: 77 :	: 10 :
	: 100 :	: :	: :	: :	: :	: :	: :
22	: n-Amyl, :	: 10.8 cc. :	: - :	: 16 :	: 50 :	: 87.6-7.9 :	: 8-9 :
	: 48 :	: :	: :	: :	: :	: :	: :
22	: n-Amyl, :	: 15.4 g. :	: - :	: 22 :	: 70 :	: 109.5-110.5 :	: 21.5 :
	: 35 :	: :	: :	: :	: :	: :	: :
21	: n-Hexyl, :	: 14.7 g. :	: 5, water bath :	: 13.5 :	: 44 :	: 107-8 :	: 16 :
	: 18 :	: :	: :	: :	: :	: :	: :
24	: n-Heptyl, :	: 17 g. :	: 6, water bath :	: - :	: 71 :	: 117 :	: 10 :
	: 40 :	: :	: :	: 16 :	: 50 :	: 137 :	: 11 :
24	: n-Octyl :	: - :	: - :	: :	: :	: :	: :
12.6	: n-Nonyl, :	: 8.8 g. :	: 5, water bath :	: 11 :	: 50 :	: 153-4 :	: 20 :
	: 15 :	: :	: :	: :	: :	: :	: :

The constants obtained by previous investigations with these esters are reviewed.

48. J. W. Walker, J. Chem. Soc. 67, 914-25(1895), "The Ethereal Salts of the Optically Active Lactic, Chloropropionic and Bromopropionic Acids".--The dry silver salt (45 g.) of d-lactic acid was added slowly to 66 g. of methyl iodide. Reaction was vigorous. The mixture was finally heated a short time on the water bath. Distilled at 200 mm., 12 g. passed over at 105.5-106°. $d_4^{13} = 1.100$.

In a similar manner, 90 g. silver salt of l-acid and 150 g. ethyl iodide yielded 29 g. ethyl l-lactate, boiling at 67-64° at 25-22 mm.

Silver salt of d-acid (25 g.) and 38 g. propyl iodide yield 6 g. of propyl lactate, $b_{150} 122-3^\circ \text{C}$.

49. J. W. Walker, S. Smiles, and M. V. Dover, Optical Activity and the Product of Asymmetry: J. Physic. Chem. 13, 574-84; C.A. 3, 2975(1909). Me lactate ($b_{35} 60-1^\circ$ $d_{20} 1.0895$; $d_{70} 1.0335$) and ethyl lactate ($b_{37} 68-9^\circ$; $d_{20} 1.0300$; $d_{70} 0.9751$) were prepared by esterification, using sulfuric acid. $d_{10} = 1.1005$; 30° , 1.0785; 40° , 1.0670; 50° , 1.0560; 60° , 1.0450 for Me ester.
50. J. Wislicenus, Studien zur Geschichte der Milchsäure und ihrer Homologen: Ann. 125, 41-70(1864).

Di-sodium lactate and its methylation with methyl iodide were studied.

When ethyl alcohol vapors were passed through lactic acid maintained at 170-180°, alcohol, water, ethyl lactate and some lactic acid distilled over. Treatment of ethyl lactate with acetyl chloride yielded ethyl acetoxypionate boiling at 176-7° (733 mm); $d_{17} 1.0458$. Ethyl acetoxyp-

propionate was decomposed by heating with 2 volumes of water at 150°; Several products, including acetoxypionic acid were obtained. Salts of acetoxypionic acid were prepared.

51. C. E. Wood, Rotatory Dispersion of Certain Derivatives of Hydroxy Acids: J. Soc. Chem. Ind. 46, 424-7T(1927); CA 22, 1572 (1928)

The esters of l-lactic acid from methyl to nonyl show increased rotation with shorter wave length. Irregularities in the molecular rotations suggest that the ester grouping has a spiral form with six atoms in the spiral.

52. C. E. Wood and S. D. Nichols, A study of the Anomalous Rotatory Dispersion of Configuratively Related Compounds: J. Chem. Soc. 1928, 1712-27.-- Configuration of methyl lactate was discussed, but no preparative data given.

B. PREPARATION AND PROPERTIES OF ETHYL LACTATE

1. B. Prager and P. Jacobson. Beilstein's Handbuch der Organischen Chemie, Vierte Auflage (Literature to Jan. 190), Vol. III, p. 264. Ethyl d-lactate has been prepared by heating the silver salt of d-lactic acid with ethyl iodide, and by heating d-lactic acid with ethanol in a sealed tube at 170° C. (Klimenko, J. Russ. Phys. Chem. Soc. 12, 25). Purdie and Williamson (J. Chem. Soc. 69, 827) prepared ethyl lactate from the zinc ammonium salt of d-lactic acid, ethanol and sulfuric acid; b_{36} 69-70° C., D_4^{14} 1.0415. Walker (Chem. Zentralblatt 1909. II. 2118) reported the following: D^{20} 1.0300; D^{70} 0.9751.

Purdie and Irvine (J. Chem. Soc. 75, 486) prepared ethyl methoxypropionate from ethyl iodide and the silver salt of d-methoxypropionic acid; b_{12} 46°; D_4^{20} 0.9551. They also prepared ethyl ethoxypropionate in a similar manner; B_{16-19} 58.5-60° C. D_4^{20} 0.9355.

Purdie and Williamson (J. Chem. Soc. 69, 828) prepared ethyl acetoxypropionate by treating ethyl d-lactate with acetyl chloride; b_{15} 76-8° C; D_4^{14} 1.0513.

Walker (J. Chem. Soc. 67, 917) made ethyl l-lactate from the silver salt of l-lactic acid and ethyl iodide; b_{22-25} 64-70°. (Compare Purdie and Lander, J. Chem. Soc. 73, 296).

Ethyl dl-lactate was made by passing ethanol vapors through lactic acid heated at 170-180° (Wislicenus, Ann. 125, 58). It was prepared by heating lactic acid to 140-150°, then treating the residue with ethanol in a sealed tube at 160-170° (Friedel and Wurtz, Ann. Chim (3) 68, 102; Schreiner, Ann. 197, 12). Lactic acid (100 g.) was dried for 48 hours on water bath and then treated with 200 g. ethanol and 75 g. dry copper sulfate and then refluxed for 24 hours (Clemmensen and Heitman, Am. Chem. J. 42, 328). Strecker (Ann. 91, 355) prepared ethyl lactate by heating calcium lactate with potassium ethylsulfate. Lactates, ethanol, and the calculated quantity of mineral acids have been used (Chem. Fabr. Gustrow, Ger. 171,835; Chem. Zentralblatt 1906, II, 470). Ethyl lactate has been prepared by 24 hours heating of ethyl chloro-propionate, sodium lactate and ethanol (Aristow, Demjanow, J. Russ. Phys. Chem. Soc. 19, 262; Ber. 20, Ref. 697). Boiling points: 154.5 at 760 mm.; 153-4°; D^0 1.0546, D^{19} 1.0308, D^{60} 0.9854, D^{91} 0.9531. Products obtained by heating ethyl lactate in a sealed tube at 250° are ethyl lactylactate and lactide (Jungfleisch, Godchot, Compt. rend. 144, 425).

Ethyl lactate is readily hydrolyzed with water (Schreiner, Ann. 197, 12). Rates of hydrolysis are given by Findlay and Hickmans (J. Chem. Soc. 95, 1010).

When treated with $SbCl_5$ in boiling chloroform, ethyl lactate yields $CH_3CH(OSbCl_4)COOEt$ (Rosenheim and Loewenstamm, Ber. 35, 1123).

Et 2, 2-dimethyl-3-hydroxybutyrate, valerolactone, lauryl caproate, Bu stearate, cyclohexyl caproate, Et caproate, is effected in the presence of a catalyst contg. essentially oxides of Cu, Cr, and of one of the group of Ba, Ca and Mg.

4. Aristow and Demjanow. J. Russ. Phys. Chem. Soc. 19, 263; Ber. 20, Ref. 698. Oxidation of ethyl lactate with acid permanganate yielded ethyl pyruvate.
5. Helge Aspelund. CA 33, 6802 (1939). Formation of dioxooxazolidines from substituted dialuric acids. Acta Acad. Aboensis, Math. et Phys. 11, No. 7, 4 pp. (1938). It was previously reported that the action of alkali on some substituted dialuric acids resulted in cleavage products described as bis-(α -hydroxy acid) ureides. Further investigations meanwhile have established these compds. as substituted 2,4-dioxooxazolidines. It is shown that a dialuric acid substituted in the 1,5-positions with hydrocarbon radicals splits to form an α -hydroxy acid monoureide when there is not an excess of alkali. With an excess of alkali the dialuric acid as well as the monoureide are converted to the 2,4-dioxooxazolidine.
6. Helge Aspelund. Acta Acad. Aboensis Math. et Phys. II, No. 14, 14 pp. (1939). Formation of dioxooxazolidines from α -hydroxy acid esters. Substituted 2,4-dioxooxazolidines are formed easily and in good yield by the action of equiv. quantities of urea and Na alcoholates on α -HO-acid esters. These compds. show no m.-p. lowering when mixed with the products obtained from treating dialuric acid derivs. with caustic. (See preceding abstr.). The hydrolysis of 5-phenyl-2,4-dioxooxazolidine under different conditions with varying quantities of caustic and with water and $(\text{NH}_4)_2\text{CO}_3$ is shown. 2,4-Dioxooxazolidine is prepd. by heating a mixt. of 10 g. of Et glycolate with equiv. quantities of Na and urea in 50 cc. of alc. After evap'tg. the alc. the residue is dissolved in water and washed once with ether. Ether residue, 0.24 g. The water soln. is treated with 7.3 cc. of concd. HCl and extd. with ether. Ether residue, 6.5 g., m. 84-6°; recrystd. from alc., m. 89-90°. In a similar way 5-methyl-2,4-dioxooxazolidine was prepd. from Et lactate. 5-Ethyl-2,4-dioxooxazolidine, m. 54.5-5.5°, from Et-CH(OH)CO₂Et. 5,5-Dimethyl-2,4-dioxooxazolidine, m. 77°, from Me₂C(OH)CO₂Et and 5,5-diethyl-2,4-dioxooxazolidine, m. 78-9°, from Et₂C(OH)CO₂Et.
7. S. Astin and H. L. Riley, Selenium dioxide. A New Oxidizing Reagent. IV. Preparation and Properties of Ethyl Ketohydroxy-succinate: J. Chem. Soc. 1934, 844-8; C.A. 23, 5409 (1934) cf. C.A. 27, 3193.

When treated with selenium dioxide, ethyl lactate gave only a trace of ethyl pyruvate; apparently $\text{OHCCOCO}_2\text{CH}_2\text{CH}_3$ or $\text{OHCCHOHCO}_2\text{CH}_2\text{CH}_3$ were formed.

- 7a. K. S. Bai, Raman Spectra of Some Carboxylic Acids: Proc. Indian Acad. Sci. 11A, 212-28 (1940); CA35, 31 (1941). The spectra obtained from

various acids, lactic acid and ethyl lactate were investigated. Lactic acid is in a monomeric state even at room temperature.

8. L. F. Audrieth and J. Kleinberg. Ammonolysis of CA33, 1662 (1939). Acid catalysis in Liquid Ammonia. III. The Effect of alpha-substituents on the Ammonolysis of Esters. J. Org. Chem. 3, 312-16 (1938); cf. C. A. 32, 4059².-- The ammonolysis of ACOEt, CNCH₂CO₂Et, CH₂(CONH₂)CO₂Et, CH₂(CO₂Et)₂, MeCH(OH)CO₂Et, PhCH(OH)CO₂Et, PhCH₂CO₂Et and EtOCH₂CO₂Et was studied at 0°; the catalytic effect of the addn. of NH₄Cl was also detd. in each case. The concept of acid catalysis has been shown to be generally applicable to the ammonolysis of the esters in liquid NH₃, the reactivities of which parallel, quantitatively, the reactivities of esters toward alk. hydrolysis in aq. soln. The relative influence of various alpha-substituents on the reactivity of the ester toward ammonolysis in liquid NH₃ is given by the following series: CN H₂NOC EtO₂C Ph(HO) Me(HO) EtO Ph H. A convenient method for the prepn. of alpha-HO amides by the action of anhyd. liquid NH₃ on the esters has been developed. Thus, to 40 g. (0.22 mol.) of PhCH(OH)CO₂Et, cooled in solid CO₂Et, cooled in solid CO₂-Me₂CO, was added 100 cc. liquid NH₃; the mixt. was stirred and allowed to remain in a steel bomb in an autoclave for 24 hrs.; the excess NH₃ was allowed to escape from the bomb and the reaction product treated with 100 cc. abs. Et₂O, filtered, washed and dried, giving 27 g. (80.5%) of mandelamide. Similarly, 59 g. (0.5 mol.) MeCH(OH)CO₂Et and 200 cc. liquid NH₃ gave 31.5 g. (70.8%) lactamide; with 4 g. NH₄Cl, the yield increases to 74-6%.

9. W. J. Bannister (to Commercial Solvents Corp.), Aliphatic esters of Carboxylic Acids: U.S. 2,029,694, Feb. 4, 1936; CA. 30, 1807 (1936); Cf. CA 29, 6902. Methyl, ethyl and butyl lactates are prepared from the alcohols and lactic acid by introducing the alcohol into the acid at temperatures ranging from the boiling point of the formed ester to approximately 20° below said boiling point and removing the resulting vapors of the formed ester, water and excess alcohol.

10. W. J. Bannister (to Commercial Solvents Corp.), Esters: U.S. 1,695,449, Dec. 18, 1928; C.A. 23, 846 (1929). In forming esters such as ethyl lactate an alcohol and an acid such as ethanol and lactic acid are heated in the presence of a liquid, e.g., benzene, and in the presence of a solid dehydrating agent, e.g., anhydrous aluminum sulfate.

11. C. M. Bean, J. Kenyon, and H. Phillips, Walden Inversion Reactions of d-(+)-alpha-p-toluenesulfonylpropionic Acid and Amide and their Derivatives: J. Chem. Soc. 1936, 303-11; C.A. 30, 3784 (1936). Many lactic acid derivatives, including acetoxypionamide, benzoyloxypionamide, benzoyloxypionyl chloride, and acetoxypionamic acid, were prepared.

Ethyl 1-lactate (20g) was hydrolyzed with 8g. NaOH and minimum quantity of water. The acid was separated and converted into acetoxypropionic acid by treatment with acetyl chloride.

Ethyl 1-lactate also was treated with ammonia to prepare lactamide.

Ethyl 1-lactate (17g.), 40 g. ethyl iodide, and 28g. silver oxide were heated for 2 hrs. The resulting ethyl 1-ethoxypropionate was hydrolyzed with NaOH; yield of ethoxypropionic acid was 12g.

d-Chloropropionyl chloride was prepared from ethyl 1-lactate and thionyl chloride.

12. G. Berger, Constitutive Influences in Ester Saponification catalyzed by Acids: *Rev. trav. chim.* 43, 163-77 (1924); *C.A.* 18, 2128 (1924) The hydrolysis of ethyl lactate and other esters was studied.
13. E. C. Bingham and H. J. Fornwalt, Chemical Constitution and Association: *J. Rheol.* I, 372-417 (1930) *C.A.* 24, 5191 (1930) The fluidity and density of ethyl lactate and of other liquids were measured.
14. C. Bogin and H. L. Wampner. Nitroparaffins as Solvents in the Coating Industry: *Div. Paint, Varnish and Plastics Chemistry. Memphis Meeting. Am. Chem. Soc. Apr. 1942, Briefs*, pp. 9-16. Ethyl lactate was used in preparing aeronautical dope.
15. B. T. Brooks, (to Standard Alcohol Co.) Hydroxy Aliphatic Esters: *U.S.* 2,176,201. Oct. 17, 1939; *C.A.* 34, 1033 (1940). Reaction is effected between methyl formate or of a hydroxy lower molecular weight saturated fatty acid and an aliphatic alcohol containing not more than 5 carbon atoms (suitably MeOH at 100-140° under pressure).
- 15a. N. von der Brüggén, Ueber den Diäthylather einer Dimilchsaure; *Ann.* 148, 224-35 (1868). When ethyl lactate is made from lactic acid and ethanol in a sealed tube the yield is not over approximately 50% unless a large excess of ethanol is used. A better yield of ethyl lactate was obtained by heating lactic acid at 140-150° to remove water, and then allowing this product and ethanol (2 or 3 volumes) to react in a sealed tube at 150-160°. From the equation given, it appears that von der Bruggen believed the main reaction occurred between lactic acid and ethanol:



16. O. Burkard and L. Kahovec, Raman Effect. LXXXII. Nitrogen Compounds. 10. (alpha-Amino and alpha-hydroxy-propionic Acids and their Esters: *Monatsh.* 71, 333-45 (1938); *C.A.* 32, 8270 (1938) Raman spectra of lactic acid and its methyl, ethyl, isopropyl and butyl esters are recorded. Raman spectra for the corresponding alpha-methoxy-propionates are included.

Isopropyl lactate (b.p. 158.6° to 161° at 760 mm) was prepared by heating lactic acid ("Lactylmilchsaure") and isopropyl alcohol at $160-170^{\circ}$ in a sealed tube for 4 hrs.

17. R. Burns, D. T. Jones, and P. D. Ritchie, Studies in Pyrolysis. I. The Pyrolysis of Derivatives of alpha-acetoxypionic Acid, and Related Substances: J. Chem. Soc. 1935, 400-406. Ethyl lactate and benzyl alcohol in equimolar proportion were heated during 20 hrs. from 150 to 200° , about 90% of the theoretical amount of ethanol being eliminated; the residue was fractionated. The yield of benzyl lactate boiling at 134° (4mm.) was 75% ($n_D^{23.5}$ 1.5049; d_4^{20} 1.1355) was 75% of the theoretical.
18. R. Burns, D. T. Jones, and P. D. Ritchie, Studies in Pyrolysis. I. The Pyrolysis of Derivatives of Acetoxypionic Acid, and Related Substances: J. Chem. Soc. 1935, 400-6. The preparation and pyrolysis of ethyl acetoxypionate was described, together with similar experiments.
19. A. Butlerow, Ueber die Aethylmilch säure: Ann. 118, 325-330 (1861)
20. Chem. Fabrik. Gustrow, Ger. 171,835, Chem. Zentr. 1906, II, 470 Lactic acid is purified through the ethyl ester, which is prepared from lactic acid salts, ethanol, and the theoretical quantity of lactic acid.
21. Chemische Fabrik auf Actien, Lactic acid esters: Brit. 256,587, Aug. 7, 1925; C. A. 21, 2906 (1927). A lactic acid salt such as calcium or magnesium lactate is treated with an alcohol (methanol or ethanol) in the presence of an acid such as sulfuric at a temperature below the boiling point of the alcohol used.
22. L. J. Christmann (To American Cyanamide Co.), Esters from Nitriles: U.S. 1,790,262, Jan. 27, 1931 C. A. 25, 1260 (1931). In forming an ester such as ethyl lactate, lactonitrile and alcohol are treated with inorganic acid generated in situ (i.e. $H_2SO_4 + CaCl_2$).
23. B. Ciocca and A. Semproni. Esterification of hydroxy acids and polyalcohols. Ann. Chim. applicata 25, 319-23 (1935).--The principle of Thielpappe (cf. C. A. 28, 108⁵) has been extended to the esterification of HO acids and polyals. Instead of H_2SO_4 , a sulfonic acid such as $PhSO_3H$, $MeC_6H_4SO_3H$, $C_{10}H_7SO_3H$ and camphor-sulfonic acid, was used. The Et esters of lactic, tartaric, citric and ricinoleic acid, and glycol and glycerol stearates were prepd. with yields up to 95%. The formates cannot be prepd. by this method as HCO_2H is decompd. by CaC_2 . (CA, 30:4, p.1028⁹, '36)
24. W. Ciusa, Oxidation of alpha-hydroxy Acids: Atti accad. Lincei, Classe sci. fis., Mat. Nat. 25, 632-7 (1937); C.A. 32, 5785 (1938). Ethyl pyruvate was obtained in 33% yield from ethyl lactate by oxidation with bromine and water.

25. H. V. Claborn and L. T. Smith. The Acetylation of Lactic Esters by Ketene: J. Am. Chem. Soc. 61, 2727-8 (1939). The acetylation of ethyl and other lactates was studied.
26. E. Clemmensen and A. H. C. Heitman, Ureides and Cyanamides of the Oxy Fatty Acids (Second Paper); Am. Chem. J. 42, 319-340 (1909). A method recommended by Bogojawlensky and Narbutt (Ber. 38, 3344) was modified and found useful for preparing esters of alpha-hydroxy acids.

"It was only when no sulfuric acid was used and the copper sulfate was dehydrated at so low a temperature that no decomposition took place that we obtained good yields of the esters. The operation was carried out as follows: The dried acid was dissolved in commercial absolute alcohol and boiled with anhydrous copper sulfate for about 24 hrs. In dehydrating the copper sulfate care must be taken to do it at as low a temperature as possible, so that no decomposition, with formation of sulfuric acid anhydride, takes place. The reaction product was then filtered, the alcohol distilled off and the ester rectified.

The yield was good for all 4 acids, and the method seems to be especially adapted to the preparation of esters easily decomposed by water, which is the case with most of the esters of the oxy fatty acids, and to be able to displace the more or less tedious processes now in use for the preparation of these esters.

Thus the operations consisting in (1) heating the potassium or silver salt with alkyl iodides, (2) heating the halogen substituted fatty acids with sodium acetate and absolute alcohol, and (3) heating the anhydrides with absolute alcohol all require to be carried out under pressure, while another method much used, distillation of the calcium salts with potassium alkyl sulfate, gives very unsatisfactory yields."

Ethyl glycolate was made by boiling 100 g. glycollic acid and 200g. commercial absolute alcohol with 75g. anhydrous copper sulfate for 24 hrs. The copper sulfate was then filtered and the ester rectified; yield, 95g. ester boiling at 158-160°.

Ethyl lactate: 100g. of 75% lactic acid was dried on steam bath for 48 hrs., then mixed with 200cc. absolute alcohol and 75 g. anhydrous copper sulfate and boiled for 24 hrs.; rectified ester boiled at 153-5°C. (yield 70g.).

27. E. G. Corbett, Esters: Australia 20, 517/34, Dec. 12, 1935; C. A. 30, 3835 (1936). Esters of lactic, tartaric and stearic acids are made by distilling a mixture of ethanol and the acid in the presence of a catalyst such as a bisulfate or sulfate of an alkali metal. The water produced is removed in stages during the distillation operation.

28. J. B. Dickey and J. G. McNally, Cellulosic Compositions of Matter Containing Organic Ester Amides: U.S. 2,253,064, Aug. 19, 1941. Ethyl lactate was used with other solvents in a plastic composition containing cellulose acetate propionate.
29. T. H. Durrans and D. G. Davidson, Plasticizers in Cellulose Ester Plastics: Chem. and Ind. 1936, 162-9; C. A. 30, 3116 (1936) The rate of evaporation of ethyl lactate and other solvents from solutions of 1/2 sec. cellulose nitrate was measured and the percentage of solvent plotted against time.
30. H. V. Euler and C. Martius, Enzymic Oxido-reduction by Yeast Dehydrogenase: Arkiv Kemi, Mineral, Geol. 11B, No. 22, 6 pp.; C. A. 28, 2739 (1934) Yeast dehydrogenase dehydrogenatus lactylglycine more slowly, ethyl lactate still more slowly, and ethanol more rapidly than lactic acid.
31. Findlay and Hickmans J. Chem. Soc. 95, 1010 The rate of hydrolysis of ethyl lactate was studied.
- 31a. Frankland and Henderson, Proc. J. Chem. Soc. 11, 54 (1895).
32. Friedel and Wurtz, Ann. Chim. (3), 63, 102.
33. E. Fourneau and G. Florence, Some Compounds of Chloral: Bull. Soc. Chim. (4) 47, 350-6 (1930) C. A. 24, 3989 (1930) The addition product of ethyl lactate and chloral was studied; it is toxic.
34. Pl F. Frankland and W. E. Garner, The Action of Thionyl Chloride on Lactic Acid and Ethyl Lactate: J. Chem. Soc. 105, 1101-1115 (1914). When a large excess of thionyl chloride is not used, the reaction with ethyl lactate yields ethyl thionyl lactate $\text{SO}(\text{OCH}(\text{CH}_3)\text{COOEt})_2$. Excess of thionyl chloride produces ethyl sulfinyl lactate $\text{CH}_3\text{CH}(\text{SO}_2\text{Cl})\text{COOEt}$. The original must be consulted for the numerous details given.
35. K. Freudenberg, H. Eichel, and F. Leutert, Syntheses of Derivatives of Amino Acids: Ber. 65B, 1183-91 (1932) C. A. 26, 5071 (1932). Following are described: ethylazidoacetyl lactate, azidoacetyl lactic acid, and related compounds.
36. K. Freudenberg and O. Huber, Steric series- V. Transformation of d-lactic acid into l-alanine: Ber. 58B, 148-50 (1925) C. A. 19, 1407 (1925) Alanine was prepared by treating ethyl toluenesulfonyllactate with ammonia.
37. K. Freudenberg and L. Markert, Steric Series, VIII. The Configuration of alpha-Bromopropionic Acid: Ber. 60B, 2447-2458 (1927) C. A. 22, 943 (1928); cf. C. A. 20, 1056. Rotations given of following active compounds: derivatives of chloropropionic acid; methoxypropionic acid,

chloride, methyl and propyl esters, amide and dimethylamide; acetoxypionic acid, chloride, methyl, ethyl and propyl esters, amide and dimethylamide; benzoyloxypropionic acid chloride, methyl ester, dimethylamide, and diethylamide; toluenesulfonyllactic acid chloride, amide, dimethylamide and diethylamide.

Ethyl d-lactate was prepared by the method of Wood, Such and Scarf (J. Chem. Soc. 123, 606 (1923)) from zinc ammonium lactate, alcohol and H_2SO_4 .

Methoxypropionic acid (45% yield) was prepared from potassium lactate and methyl sulfate.

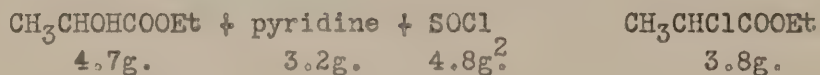
Acetoxypionic acid was prepared in 84% yield by the method of Anschutz (Ber. 37, 3972 (1904). B.p. 125-127° at 10 mm.

Benzoyloxypropionyl chloride was prepared by the method of B. Helferich and L. Keiner (Ber. 57, 1618 (1924)).

38. K. Freudenberg and M. Meister, Steric Series. XXII. Configuration of Alanine: Ann. 518, 86-96 (1935); C. A. 29, 6210, (1935); cf. C. A. 28, 6110, 22, 943. The following were prepared: carbethoxy lactic acid, following were prepared: carbethoxy lactic acid, chloride, ethyl ester, phenyl ester, dimethyl amide, and anilide. Also the following: ethanesulfonylpropionic acid derivatives: chloride, phenyl ester, dimethyl amide, and anilide.
39. K. Freudenberg and F. Rhino, Die Konfiguration des Alanins: Ber. 57, 1547-1557 (1924).--Using a method previously described (E. Fischer and A. Speier, Ber. 28, 3255 (1895); K. Freudenberg and F. Rhino, Ber. 56, 199 (1923)), methyl and ethyl lactates were prepared in approx. 60% yield. The following were prepared: ethyl d-acetoxypionate (80% yield); ethyl hexahydrobenzoyloxypropionate; methyl benzoyloxypropionate (70%); benzoyloxypropionamide; methyl toluenesulfonyllactate; ethyl toluenesulfonyllactate; toluenesulfonyllactate (65% yield); and corresponding derivatives of alanine.
40. H. A. Gardner, Ethyl Lactate: Paint Manufacturer's Assoc. of U. S., Circ. No. 225, 176-8 (Jan. 1925); C.A. 19, 1060 (1925). A sample of ethyl lactate had density of 1.0385, flash pt. 117°F. (closed cup) and boiling point approximately 150°. It dissolved low-viscosity nitrocellulose very readily to produce a solution of somewhat greater viscosity than a similar solution made with butyl acetate, but the former can be diluted with non-solvents such as benzene to a very much greater extent than the latter before the cellulose ester is thrown out.
41. W. Gerrard, The esters of Sulfurous, Chlorosulfinic, and Chlorosulfonic Acid. III. J. Chem. Soc. 1940, 218-230 (C.A.34, 2811 (1940) cf. C. A. 33, 2483⁵). Pyridine and ethyl chlorosulfinoxypropionate react to give

55% of ethyl chloropropionate. Ethyl lactate and SO_2Cl_2 gave ethyl chlorosulfonxypropionate in 65% yield. The carbonate was prepared in high yield from phosgene and ethyl lactate.

42. Wm. Gerrard, Esters of Sulfurous, Chlorosulfinic and Chlorosulfonic Acid: J. Chem. Soc. 1939, 99-103; C. A. 33, 2483 (1939). Thionyl chloride and ethyl lactate give 84% of alpha-carboethoxy sulfite. Ethyl alpha-chloropropionate is easily prepared from this compound.
43. W. Gerrard, J. Kenyon, and H. Phillips, The Replacement of the Hydroxyl Group of Ethyl (+) Lactate by Halogens, and the Molecular Dissymetry of Derivatives of Ethyl Lactate which contain the Sulphin Group: J. Chem. Soc. 1937; 153-158



44. P. K. Glasoe and L. F. Audrieth, Acid Catalysis in Amines. I. The Catalytic Effect of Cyclohexylammonium Salts on the Reaction between Cyclohexylamine and Esters: J. Org. Chem. 4, 54-9 (1939) C. A. 33, 4206 (1939). Cyclohexyllactamide was prepared from ethyl lactate.
45. J. W. E. Glattfeld and D. Macmillan, Lactones in Liquid Ammonia: J. Am. Chem. Soc. 58, 898-901 (1936). Methyl, ethyl, propyl and butyl lactates were ammonolyzed by liquid ammonia.
46. M. Godchot and P. Vieles, Racemic and Active Methylglycolic Acids and their Derivatives: Bull. Soc. Chim. (5) 4, 937-44 (1937); C. A. 32, 112 (1938); cf. C.A. 30, 4818. Treatment of the sodium derivative of ethyl lactate with ethyl chloroacetate yielded ethyl methyl-diglycolic acid. Ethyl lactate boils at 58° at 20 mm.; d_4^{20} 1.033; n_D^{20} 1.4125.
47. M. Godchot and P. Vieles, An Attempt to Prepare an Optically Active Diacid Ether by Means of Asymmetric Compounds: Bull. soc. chim. (5) 5, 1535-9 (1938); C.A. 33, 1666 (1939). Interaction of ethyl alpha-bromopropionate with the sodium derivative of ethyl lactate yields ethyl dilactylate in large amounts.
48. H. Gorgeot, Lactic Acid Esters: Fr. 678,627, Nov. 12, 1928, C. A. 24, 3516 (1930). The dry alkaline earth lactate is treated with alcohols in the presence of mineral acid just sufficient to liberate the lactic acid.
49. E. S. Greigov. Use of Lactates as Solvents. Peintures, pigments, vernis 16, 141-3 (1939). The Et, Bu and Am esters of lactic acid have excellent solvent power for nitrocellulose, cellulose acetate and various varnish resins and are useful in formulating lacquers, which may contain drying oils. (C.A., 34:12, p. 4289⁹, '40).

50. R. Grütter and H. Pohl, Making Esters of Lactic Acid or Similar Fatty Acids: U. S. 1160,595, Nov. 16, 1915; C. A. 10, 251 (1916). Lactic acid is heated to 107-180° while passing air through it to form anhydride and the latter is then heated under a reflux condenser with alcohol containing 2% of HCl to promote the formation of lactic ester. Instead of HCl, aluminum sulfate, or titanate compounds or anhydride may be used to accelerate the formation of lactic, glycolic or similar esters.
51. Frank Hartwich, to Schering-Kahlbaum A.-G., Lactic Acid Esters: Ger. 518,388, Jan. 23, 1926. C.A. 25, 2437 (1931). A mixture of magnesium lactate, an alcohol, and an acid, with or without a catalyst, e.g. an excess of acid or calcium chloride, is heated.
52. A. Haussler (to C. H. Boehringer & Sohn Chemische Fabrik) Manufacture of Esters of Oxy Acids: U.S. 1,614,195, Jan. 11, 1927. Ethyl lactate (120g.) was passed over 400 g. vanadium pentoxide at 250°C. About 70g. of distillate containing 70% of the ethyl ester of pyroracenic acid.
53. B. Helferich and L. Keiner, Preparation of Higher Ketones: Ber. 57B, 1616-20 (1924); C.A. 19, 466 (1925). The following were prepared: Benzoyloxypropionyl chloride, ethyl acetylactylallylacetoacetate, and ethyl benzoyllactylacetoacetate. On hydrolysis of the acetoacetates, the expected hydroxy ketones were not obtained.
- Lactic acid (15g.) was heated with 21g. benzoyl chloride for 1/2 hr. at 100°; the product was dissolved in hot sodium carbonate solution, and precipitated with HCl. The crude benzoyloxypropionic acid was treated with thionyl chloride; yield 35%.
- 53a. Homfray and Guye, J. Chim. Phys. I, 519,- Physical constants.
54. J. Houben and E. Dfankuch, Hydroximido--and alpha-hydroxyhydroximido Acid Esters: Ber. 59B, 2397-2402 (1926) C.A. 21, 388 (1927) Compounds such as the following were prepared: $\text{CH}_3\text{CHOHC}(\text{:NH.HCl})\text{OCH}_2\text{CH}_3$; ethyl imido lactate; ethyl lactohydroximate; beta-chlorolactonitrile:
55. J. Houben and W. Fischer, Process for the Catalytic Esterification of Alcohols in Alkaline Solution: Ber. 64B, 240-7 (1931) C.A. 25, 3311 (1931). Ethyl benzoyl lactate was prepared from trichloroacetophenone and ethyl lactate in the presence of alkali alcoholate. Yield: 76%
56. W. R. H. Hurtley and T. S. Wheeler, Lactic Esters: Brit. 346,486, Jan. 25, 1930; C.A. 26, 1940 (1932). Butyl lactate is prepared from ethyl lactate and butanol in the presence of strong acid.
57. Imperial Chemical Industries, Ltd., and W. R. H. Hurtley, Lactic Acid and its Esters: Brit. 341,961, Oct. 25, 1929; C.A. 25, 4893 (1931).

HCN is condensed with acetaldehyde in the presence of an alcohol or of a lactic acid ester, and an inorganic acid such as dry HCl is then added to form lactic acid or, in the presence of alcohol, the lactic ester. Details are given for the preparation of lactic acid and ethyl lactate.

58. Imp. Chem. Ind. Ltd., W. R. H. Hurtley and T. S. Wheeler, Lactic Esters: Brit. 346,486, Jan. 25, 1930. C.A. 26, 1940 (1932). Butyl lactate was prepared from ethyl lactate and butanol.
- 58a. Jones and Neuffer, J. Am. Chem. Soc. 39, 659 (1917) - Action of hydroxylamine on ethyl lactate.
59. E. Jungfleisch and M. Godchot, On Ethyl Lactyllactates: Compt. rend. 144, 425-7; C.A. I, 1387 (1907). When ethyl lactate was heated for 8 hrs. at 250°, it was converted into a mixture of ethyl lactyllactate and lactide. Ethyl lactyllactate boils at 215-220°; $d_4^{20} = 1.066$ (see Wurtz and Friedel, Ann. chim. phys. (3) 63, 112).
60. Jungfleisch and Godchot, Compt. rend. 144, 979. Ethyl chloropropionate and the sodium derivative of ethyl lactate yielded the ether ester; hydrolysis of this ester gave dilactylic acid (m.p. 105-7°). The ether acid has been made by heating calcium lactate to 280° (see Wurtz and Friedel, Ann. chim. phys. (3) 63, 114; Ber. 23 Ref., 325).
61. Jungfleisch and Godchot, Compt. rend. 145, 71. Interaction of the sodium derivative of ethyl lactate and ethyl chloroacetate yielded the expected ether ester; subsequent hydrolysis gave the acid (m.p. approx. 80°).
62. Felix Kaufler and Hilger P. Schmitz (to Alex. Wacker Ges. für elektrochemische Industrie, G. m. b. H.). U.S. 2,102,957, Dec. 21. Stable asphalt solutions suitable for use in coating, binding or impregnating various materials. Gilsonite or Syrian asphalt is used with a solvent comprising at least 90% of paraffinic hydrocarbons b. 50-200°, the solvent action of which is increased by an admixt. of less than 10% of diacetone-alc., butyleneglycol-beta-ethyl ether, BuOH, Bu glycolate, Et lactate, Et Pr ketone, acetone, acetophenone or cyclohexanone.
63. J. Kenyon, H. Phillips, and H. G. Turley, Dependence of Rotatory Power on Chemical Constitution. XXIV. Further Experiments on the Walden Inversion: J. Chem. Soc. 127, 399-417 (1925) C.A. 19, 1407 (1925). Ethyl lactate was prepared in 80% yield by treating sodium lactate with ethyl toluene-sulfonate. Alkali metal salts of acids react with ethyl toluene-sulfonyllactate to yield the acyloxypropionates. Related reactions are described.

"Several methods have been described for the preparation of ethyl lactate, but, owing to its solubility in water and to the great ease with which it undergoes hydrolysis, especially in the presence of traces of alkali, its preparation in a state of purity is rendered somewhat

tedious and difficult.

64. D. B. Keyes, S. Swann, Jr., and H. W. Hoerr, Conductivity of Organic Solvents: Trans. Am. Electrochem. Soc. 54, 7 pp. (1928) C.A. 22, 3843 (1929). The conductivities of thirteen solvents were determined:

Solvent	Cond. (reciprocal Int. ohm.-cm)
	$\times 10^{-12}$ at 25°
Cellosolve -----	1,800,000
Cellosolve acetate -----	47,000
Toluene -----	49
Butyl alcohol -----	2,900,000
Ethyl lactate -----	1,000,000

65. G. A. Kirkhgoof and K. I. Znaeva, New Method of Preparation of Ethyl Lactate: Khim. Farm. Prom. 1933, 280-1; C.A. 28, 3714 (1934). Calcium lactate (308g.) is dissolved in 600cc. hot water, 250g. of CuSO_4 in 300cc. of boiling water is added, and the copper lactate is filtered and crystallized. Copper lactate (556g.) is heated with 360g. of 96% alcohol and 1.84g. of 27% oleum with a reflux condenser until congo paper shows a neutral reaction (6-8 hrs.). The CuSO_4 is filtered and the solution fractionated at 40 mm. The yield is 64%.
66. Klimenko, J. Russ. Phys. Chem. Soc. 12, 25. Ethyl d-lactate was prepared (1) from silver d-lactate and ethyl iodide and (2) by heating d-lactic acid with ethanol in a sealed tube at 170°.
67. A. Kraus. Solvents for nitrocellulose. V. The solvent power of carbon disulfide. Farben-Ztg. 46, 190 (1941); cf. C.A. 35, 7800¹. Nitrocellulose contg. 10.48% N neither dissolved nor swelled in mixt. of equal parts by vol. of CS_2 and PrOH , BuOH , iso- BuOH , glycerol, ether, cyclohexane, benzene, $\text{C}(\text{NO}_2)_4$ or $\text{C}_2\text{H}_4\text{Cl}_2$; it was more sol. and dissolved more rapidly in mixts. of CS_2 and ethylene glycol or Et lactate up to approx. equal proportions by vol., then the soly. diminished with higher proportions of CS_2 in the mixt. Much CS_2 can be added to acetone without appreciable effect on the solvent power of the latter for nitrocellulose. (CA 36:4, p. 1174, '42)
68. G. F. R. Krige and K. Hollow, Investigation of Reaction Velocity by Means of Hydrogen Electrode. I. Alkaline Saponification of Esters: Trans. Faraday Soc. 30, 644-8 (1934) C.A. 28, 6614 (1934). The velocity of saponification of ethyl lactate with sodium hydroxide was investigated at 15°, 25.3°, and 34.9°C. and the temperature coefficient was found to be 1.82. The energy of activation was 10,500 cal.
69. W. Kuhn and H. Biller, Rotation of Chromophoric Groups in Similarly Constructed Compounds: Z. physik. Chem. B29, 1-41 (1935); C. A. 29, 5819 (1935). Absorption, rotation dispersion and in some cases circular dichroism were measured for methylcyclohexyl, methylphenyl carbinol, their

nitrites, acetates, and carbomethoxy compounds, mandelic acid ethyl ester and nitrile, the esters and dimethylamides of the methyl ethers of mandelic and atrolactic acid and the esters and dimethylamides of the carbethoxy and ethanesulfonyl compounds of lactic acid and alanine.

70. Paul Kümmler. Lactic acid esters. *Farbe u. Lack* 1938, 449-50.--Com. Et and Bu esters of lactic acid were tested for stability by boiling for a short time with water and by standing in contact with water for 2 months. The amt. of acid formed was not excessive, the stability being about equal to that of AmOAc and superior to that of BuOAc. The Et, Bu and Am esters of lactic acid did not cause livering with zinc white nor discoloration with a Cu bronze. (See *Paint, Oil and Chemical Review* 102, 26 (1940). (C. A. 33:4, p. 1523, '39)
71. A. R. Latven and H. Molitor, Comparison of the toxic, hypnotic and Irritating properties of eight organic solvents: *J. Pharmacol.* 65, 89-94 (1939); C.A. 33, 2113 (1939). Ethyl lactate is relatively toxic.
72. M. Lécat, New Azeotropes. I and III; *Ann. soc. sci. Bruxelles* 45, 169-76, 284-94 (1926); C. A. 22, 3561 (1928); cf. C. A. 21, 1583, 2834. Ethyl lactate (b. 153.9°C.) forms an azeotrope (b. 143.10°) with 50.2% alpha, alpha-dichlorohydrin, and an azeotrope (b. 144.95°) with 45% camphene. Methyl lactate (b. 143.8°) forms an azeotrope (b. 138.5°) with 56% isoamyl acetate (b. 142.1°).
73. Lepage. *J. Prakt., Chem.* 31, 377, was referred to by Strecker (*Ann.* 91, 355) in connection with ethyl lactate.
74. P. A. Levene and H. L. Haller, Conversion of optically active lactic acid into the corresponding propylene glycol: *J. Biol. Chem.* 67, 329-32 (1926) C.A. 20, 1787 (1926). Thoroughly dried calcium lactate (25g.) was suspended in 150cc. of absolute alcohol and 12g. concd. H₂SO₄ slowly dropped in, the mixture being thoroughly stirred with a mechanical stirrer. The mixture was heated under reflux condenser in an oil bath (90-100°C.) overnight. It was then cooled and neutralized with potassium carbonate, filtered and distilled at 20mm. Ethyl lactate (b. 54-56°C.) was obtained in 52% yield.
75. P. A. Levene and A. Rothen, Walden Inversion. XVIII. Analysis of Rotatory Dispersion Curves of alpha-Substituted Normal Carboxylic Acids: *J. Biol. Chem.* 107, 533-53 (1934). C. A. 29, 1063 (1935). Absorption curves obtained for lactic acid, its sodium salt and ethyl ester, methoxy lactic acid, its sodium salt and ethyl ester.
76. Barnard M. Marks (to E. I. du Pont de Nemours & Co.). Synthetic resin composition. U.S. 2,109,573, Mar. 1. A polyvinyl acetal resin is used with benzyl ether of Et lactate or a like compd. which serves as a plasticizer. P. 3052.

77. H. Martin and E. S. Salmon, The Fungicidal Proportion of Certain Spray-Fluids. XI. Synthetic Solvents: J. Agr. Sci. 24, 469-90 (1934); C.A. 28, 6515 (1934); cf. C. A. 27, 3770. Ethyl and butyl lactates were studied.
78. S. Masui, The Reactions of Various Esterases on dl-Ethyl Lactate: Acta Schol. Med. Univ. Imp. Kyoto 13, 339-53 (1931) C.A. 25, 3676 (1931). The d-ethyl lactate seems to be more strongly hydrolyzed than the l-ethyl lactate, since the zinc lactate formed always shows dextro-rotatory power.
79. H. W. Matheson and K. G. Blaikie, Hydroxy Acid Esters; Brit. 257, 907, Sept. 3, 1925; C.A. 21, 3057 (1927). Esters of hydroxy acids are prepared from cyano hydrins. Water and cyanohydrin are present in substantially equimolar proportions and the inorganic acid in proportion to combine with NH_3 . Ethyl lactate and other esters were thus prepared. The cyano-hydrins were prepared from anhydrous HCN and aldehyde or ketone in the presence of a trace of alkali or cyanide.
80. H. W. Matheson and K. G. Blaike, Hydroxy Acid Esters: Brit. 264, 143, Jan. 11, 1926; C. A. 22, 91 (1928). Substantially anhydrous esters are produced by reaction of alcohols on cyanohydrins of ketones or aldehydes in the presence of water and sufficient HCl to combine with ammonia. The preparation of ethyl lactate and other esters is described.
81. H. W. Matheson and K. G. Blaikie, Lactic Acid Ester: Can. 263, 186, Aug. 3, 1926; C. A. 20, 3696 (1926). Ethyl lactate is produced by causing acetaldehyde cyanohydrin and ethanol to react in the presence of HCl and less water than will serve to hydrolyze all the cyanohydrin to lactic acid.
82. H. W. Matheson and K. G. Blaikie, Lactic Acid Esters: U.S. 1,650,950, Nov. 29, 1927; C. A. 22, 597 (1928). Acetaldehyde cyanohydrin is caused to react with an alcohol such as ethanol in the presence of an organic acid, e.g., HCl, in sufficient quantity to combine with the liberated ammonia, and in the presence of less water than would serve to hydrolyze all the cyanohydrin to lactic acid.
- 82a. Morgan and Kramer, J. Am. Chem. Soc. 35, 1834 (1913); 39, 2261 (1917). Constants only.
83. M. H. Palomaa, Influence of the Position of the Oxygen atom in the Chain on the Velocity of Ester Hydrolysis: Ann. Acad. Sci. Fennicae. (A) 4, 1-104; Chem. Zentr. 1913, II. 1956; C. A. 8, 1772 (1914). The following lactic acid derivatives were studied; methyl lactate, ethyl lactate, methyl methoxypropionate, and ethyl ethoxypropionate.
84. L. Pauling, the Interpretation of the Infrared Absorption of Organic Molecules Containing Hydroxyl and Amino Groups: J. Am. Chem. Soc., 58,

94-8 (1936).

Proton attraction by oxygen atoms occurs in benzoin and in ethyl lactate.

85. I. Peyches, The Raman spectra of some acids and alcohols and their Derivatives; esters and salts: Bull. Soc. chim. (5) 2, 2195-2209 (1935). C. A. 30, 2492 (1936) cf. C. A. 29, 682. The Raman spectra of lactic and glycolic acids and their esters and salts were compared with acetic and propionic acids, esters, and salts, (Specific lactic esters not mentioned in Chem. Abstracts).

86. I. K. Phelps and H. E. Palmer, The Identification and Estimation of Lactic Acid in Biological Products. First Paper: J. Am. Chem. Soc. 39, 136-149 (1917). Lactic acid was esterified with ethanol containing in solution dry hydrogen chloride in the presence of zinc chloride according to the method of Phelps and Phelps (Am. J. Sci. (4) 24, 194 (1907)) for the esterification of succinic acid. The product boiled at $67-71^{\circ}$ (30mm.) and at $153.8-154.3^{\circ}$ under atmospheric pressure. It was hydrolyzed by refluxing 4 hours with a large volume of water. The lactic acid was removed from the water by ether in a continuous liquid extractor.

Using excessive quantities of ethanol, lactic acid was esterified in almost theoretical yields. Ethanol (200cc) containing 2.5g. HCl per liter was passed through 0.5 g. or less of lactic acid in the presence of 1g. zinc chloride; the esterification flask was kept at $100-110^{\circ}$, the alcohol and ester were distilled continuously, and the process lasted 1.5 hrs. The ester was hydrolyzed and determined as guanidine lactate.

87. E. J. Powers (to Commercial Solvents Corp.), Acylated Esters of Hydroxy Acids: Can. 310,854, Apr. 28, 1931. C. A. 25, 3015 (1931). A mixture of a hydroxy aliphatic acid and ester is refluxed in the presence of catalyst, e.g., HCl, H_2SO_4 , H_3PO_4 , etc.

88. T. Purdie and J. C. Irvine, The Rotatory Powers of Optically Active Methoxy and Ethoxy Propionic Acids prepared from Active Lactic Acid: J. Chem. Soc. 75, 483-493 (1899). Methyl d-lactate was prepared (37g. yield) from 120g. zinc ammonium d-lactate, 462g methanol, and 96g. sulfuric acid. $B_{19} 58^{\circ}$; $d_4^{20} 1.0925$.

The yield by this process was so small that silver salt method was preferred. From 91g. silver salt and 136g. methyl iodide was obtained 37g. of ester, boiling at $58-62^{\circ}$ under 22-33mm. pressure. Ethyl d-lactate was prepared from $ZnNH_4$ salt in comparable yield.

Silver oxide (1.5 moles) was added gradually to a mixture of 1 mole methyl lactate and 3 moles methyl iodide. Yield of crude ester was 65%.

89. T. Purdie and G. D. Lander, The Action of Alkyl Iodides on Silver Malate and on Silver Lactate: J. Chem. Soc. 73, 287-301 (1898). From 173g. silver lactate and 290g. ethyl iodide was obtained 57g. ester (55% yield) boiling at 151-4°.

From 235g. silver lactate and 358g. isopropyl iodide was obtained 40g. (25%) ester.

90. T. Purdie and G. D. Lander, Optically Active Alkyloxypropionic Acids: J. Chem. Soc. 73, 862-878 (1898). Using Schreiner's method (Ann. 197, 13 (1897)), 240g. (approx. 50%) ethyl ethoxypropionate was obtained from 580g. ethyl bromopropionate. The cause of the low yield was attributed to the formation of ethyl acrylate.

Methyl methoxypropionate (186g. or 53% yield) was made from methyl bromopropionate (500g.).

Propyl bromopropionate (200g.) was added gradually to a hot solution of 26g. sodium in 400g. propyl alcohol. Heated for 1 hr., and then treated with CO₂. Yield was 55%; b.p. 187-8°.

91. T. Purdie and S. Williamson, Ethereal Salts of Optically Active Malic and Lactic Acids: J. Chem. Soc. 69, 818-839 (1896). Silver d-lactate (85g.) and 150g. ethyl iodide gave 22g. product, b.p. 69-70° at 36mm., d_4^{14} 1.0415.

Mixture of dextrolactic acid syrup (30g.) and 120g. ethyl alcohol and 12g. of sulfuric acid were heated on water bath for 4 hours, and then neutralized and dried with dry potassium carbonate. Yield was 15g. boiling at 63-5 at 25mm. B_{43}^{71} ; d_4^{14} 1.0423.

This product was obtained more advantageously by heating 65g. dry zinc ammonium lactate, 250g. ethanol, and 50g. sulfuric acid on water bath for 4 hrs. Yield was 39g.; b_{27}^{65} .

Using acetyl chloride, ethyl d-lactate was acetylated; b_{15}^{76} 76-8°; d_4^{14} 1.0513; b_{18}^{81} ; d_4^{14} 1.0513.

Using phosphorous pentachloride (57g.) dissolved in 80g. chloroform, 32g. ethyl lactate was converted into 12g. of ethyl chloropropionate, b_{50}^{68} 68°.

92. V. von Richter, R. Anschutz, and F. Reindel, Organic Chemistry or Chemistry of the Carbon Compounds, Nordemann Publishing Co., N.Y.C., 1934, pp.415-421. Lactic acid and its methyl and ethyl esters are reviewed briefly. Lactide formation is discussed.

93. P. D. Ritchie, Studies in Pyrolysis. III. The Pyrolysis of Carbonic and Sulfurous Esters: J. Chem. Soc. 1935, 1054-61. Acyl derivatives of

lactic esters were prepared and pyrolyzed; products were acrylic esters.

94. P. D. Ritchie, D. T. Jones and R. Burns, Manufacture of Derivatives of Unsaturated Acids: U.S. 2,265,814, Dec. 9, 1941. Some of the esters prepared and pyrolyzed are: acetoxypionitrile, methyl acetoxypionate, ethyl acetoxypionate, di-(alpha-carboethoxyethyl) sulfite, di-(alpha-carbomethoxyethyl) carbonate, and methyl carbomethoxyethyl carbonate. Pyrolysis of these compounds yielded acrylic esters or acrylonitrile.

95. P. D. Ritchie, D. T. Jones, and R. Burns, Improvements in or relating to the manufacture of derivatives of unsaturated acids: Brit. 424,885, Mar. 4, 1935. Acyl derivatives of alkyl lactates were prepared and pyrolyzed; products were acrylic esters.

96. P. Rona and R. Itelsohn-Schechter, The Hydrolysis of Ethyl Esters of Lactic Acid by Liver Esterase: Biochem. Z, 203, 293-7 (1928): C. A. 23, 1426 (1929) Pig-liver esterase attacks preferably the d-form of ethyl lactate when either the racemic or either of the optically active modifications is used as substrate.

97. S. Sabetay. Some Esters of Lactic Acid: Bull. soc. chim. (4) 47, 436 (1930). C. A. 24, 3990 (1930) By treatment of lactic esters with acid chlorides in the presence of pyridine, the following new compounds were prepared:

 Ethyl phenylacetyl lactate b_g 144.5-5.5°; n_D^{21} 1.4880; d_{21} 1.096.
 Ethyl cinnamoyl lactate, b_g 172.5-3°; n_D^{21} 1.5374; d_{21} 1.106.
 Phenethyl acetyl lactate, b_g 144-7°; n_D^{22} 1.4913; d_{22} 1.099.
 Citronellyl acetyl lactate, b_3 153°; n_D^{22} 1.4479; d_{22} 0.9647.

98. E. J. Salmi and T. Suonpää, Untersuchungen Über Ätherartig Verbindungen. VII. Zum Einfluss der Chloratom auf die Geschwindigkeit der spontanen Wasserverseifung der Ester: Ber. 73, 1126-1131 (Oct. 1940). The hydrolysis of several esters, including the ones listed below, was studied:

The Relative K_s Values of esters of hydroxy acids at 25°C.

Acid Component	n-alkyl Ester	Methylene Ester	Ethylidene Ester	Trichloroethylidene Ester
Glycolic acid	91.8	-----	-----	169
Lactic acid	100	100	100	100
alpha-Hydroxyisobutyric acid	33.3	33.2	47.1	9.45
Methylethylglycolic acid	10	9.5	24.3	2.93

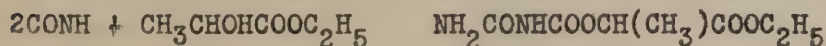
99. S. Santiago and A. P. West, Chaulmoogryl derivatives of lactates and salicylates: Phillippine J. Sci. 35, 405-9 (1928). C. A. 22, 3638 (1928). The following were prepared by treating the proper ester with chaulmoogryl chloride for 4 days at about 140-180° and crystallizing from methanol with bone black: methyl chaulmoogryl lactate (m.p. 51-4°, 38% yield) and ethyl chaulmoogryl lactate (m.p. 54-7°, 33% yield).
100. Schering-Kahlbaum A.-G., Lactic Acid Esters: Ger. 518,388, Jan. 23, 1926; C. A. 25, 2437 (1931). A mixture of magnesium lactate, an alcohol and an acid, with or without a catalyst, e.g., an excess of acid or calcium chloride, is heated.
101. Schering-Kahlbaum A.-G. Lactic Acid Esters: Brit. 319,043, June 14, 1928; C. A. 24, 2470 (1930). An inorganic acid such as sulfuric is added with cooling to a lactate such as magnesium lactate and an alcohol such as ethanol; after standing for sometime, the mixture is heated somewhat below the boiling point of the alcohol, nearly neutralized, and is then finally heated to a slightly higher temperature than before (but still below the boiling point of the alcohol), followed by cooling, complete neutralization, and isolation of the product.
102. Schering-Kahlbaum A.-G., Esters: Ger. 548,371, Oct. 10, 1929; C. A. 26, 3515 (1932). Esters prepared from acids which have been obtained with the acid of enzymes are purified by passing them in the vapor phase over or through superficially active material, e.g., active carbon or silica gel. Examples are given of the purification of ethyl lactate and methyl butyrate.
103. R. Schnurmann and E. Warlow-Davies, The Electrostatic Component of the Force of Sliding Friction: Proc. Phys. Soc. (London) 54, 14-26 (1942); C. A. 36, 2399 (1942). Data are given for observations using as lubricants ethyl lactate and esters of other acids.
104. L. Schreiner, Ueber die Siedepunkte der Ester und Aether-Ester der Oxy-sauren: Ann. 197, 1-26 (1879). Although heating lactic acid and alcohol at 150° was unsatisfactory, the same procedure at 160° gave ethyl lactate and methyl lactate in good yields. Alkoxy esters were prepared from alkyl bromopropionates and sodium alcoholate. Constants given are:

	B.p. °C.	Density		
		0°C.	19°C.	
Methyl lactate	144.8	1.1180	1.0898	1.0280(80)
Ethyl lactate	154.5	1.0546	1.0308	.9854(60)
Ethyl Methoxypropionate	135.5	.9906	.9765(18°)	.9280(66)
Ethyl ethoxypropionate	155	.9498	.9326	.8862(65)

105. F. S. Schwackhamer, (to American Cyanamide Co.) Purifying Ethyl Lactate: U.S. 2,269,402, Jan. 6, 1942. C. A. 36, 2870 (1942).

106. E. Schwenk and F. Hartwich, Esters: Ger. 548,371, Oct. 10, 1929. (to Schering-Kahlbaum A.-G.) Vapors were passed through active C or silica gel to effect purification. C. A. 26, 3515 (1932).
 107. L. T. Smith and H. V. Claborn, Lactic Esters. Preparation and Properties: Ind. Eng. Chem. 32, 692-4 (1940). Detailed directions are given for preparing methyl lactate and other esters from calcium, sodium, and zinc lactate in high yields. Sulfuric acid is used to neutralize calcium lactate. The original article should be consulted for details and physical constants of many lactic esters.
 - 107a. Steffens, U.S. 1421, 604, July 4, 1922.
 108. A. Strecker, Ueber einige neue Verbindungen der Milchsäure: Ann. 51, 352-67 (1854). Lepage's (J. prakt. Chem. 31, 377) preparation of ethyl lactate was discussed. One part of dry calcium ("Kalikalk") lactate and 1.4 parts of potassium ethyl sulfate were heated in an oil bath. At 150° a reaction occurred. The product (d 1.08) boiled at 150-160°.
- Benzoyloxypropionic acid was prepared.
109. R. W. Stoughton, 5,5-Dialkyl-2,4-oxazolidinediones: J. Am. Chem. Soc. 63 (9) 2376-2 (1941). Substituted glycolic acids (prepared from ketones and HCN) were esterified in the usual manner by refluxing with absolute alcohol saturated with dry hydrogen chloride (this did not include the prepared of lactic esters).
- Urea, ethyl lactate and sodium reacted to give 5-methyl-2,4-oxazolidinedione (81% yield).
- $$\begin{array}{c} \text{CH}_3\text{CHCONH} \\ \text{O} \quad \text{CO} \end{array}$$
110. J. Thiele and F. Dent, Zur Kenntniss der Urethane: Ann. 302, 245-272 (1898). Phosgene and ethyl lactate reacted and gave chloroformyloxypropionate, b₁₉ 91°; b₇₁₄ 180° with slight decomposition. When a benzene solution of this compound was treated with ammonia, a pour yield of carbamate was obtained.
 111. E. G. Thomssen, Flavoring Extracts Containing Ethyl Lactate as a Solvent: U.S. 1,602,183, Oct. 5, 1926; C.A. 20, 3756 (1926).
 112. Edward Thorpe, A Dictionary of Applied Chemistry, Vol. IV, 1922, pp.5-11, Longmans, Green and Co. Excellent review of the manufacture, properties, and uses of lactic acid and its salts; the methyl, ethyl, ethyldene, and glyceryl esters are described briefly.
 113. W. Traube, Ueber cingine Derivate der Allophansäure: Ber. 22, 1572-9 (1889). Vapors of cyanic acid (HOCN, "cyansäure") were passed through

on mixture of 15g. ethyl lactate and 2 or 3 volumes of absolute ether as long as absorption occurred. The crystals thus obtained were washed with ether, and crystallized from water (m. 170°). On heating the product decomposed into cyanic acid and ethyl lactate. The reaction was described as:



The new ethyl lactate derivative gave the acid ($\text{C}_5\text{H}_8\text{O}_5\text{N}_2$) and ethyl chloride in almost quantitative yield when heated with concentrated hydrochloric acid; the product ($\text{NH}_2\text{CONHCOOCH}(\text{CH}_3)\text{COOH}$) was crystallized from water; m.p. 190°. Decomposition yielded cyanic acid and lactic acid.

The amyl ester ($\text{NH}_2\text{CONHCOOCH}(\text{CH}_3)\text{COOC}_5\text{H}_{11}$) was prepared from amyl lactate and by esterification of the acid described above.

Ethyl glycolate, diethyl malate, and resorcinol were converted into similar derivatives by treatment with cyanic acid vapors. Ethyl hydroxyisobutyrate and ethyl citrate failed to react.

113a. Traube and Ascher, Ber. 46, 2077 (1913).- Ethyl lactate plus guanidine.

114. J. W. Walker, J. Chem. Soc. 67, 914-25 (1895). "The Ethereal Salts of the Optically Active Lactic, Chloropropionic and Bromopropionic Acids." The dry silver salt (45g.) of d-lactic acid was added slowly to 66g. of methyl iodide. Reaction was vigorous. The mixture was finally heated a short time on the water bath. Distilled at 200mm., 12g. passed over at 105.5-106°.

In a similar manner, 90g. silver salt of l-acid and 150g. ethyl iodide yielded 29g. ethyl l-lactate, boiling at 67-64° at 25-22mm.

Silver salt of d-acid (25g.) and 38g. propyl iodide yield 6g. of propyl lactate, b_{150} 122-3°C.

115. J. W. Walker, S. Smiles, and M. V. Dover, Optical Activity and the Product of Asymmetry: J. Physic. Chem. 13, 574-84; C.A. 3, 2975 (1909). Me lactate (b_{35} 60-1°, d_{20} 1.0895; d_{70} 1.0335) and ethyl lactate (b_{37} 68-9°; d_{20} 1.0300; d_{70} 0.9751) were prepared by esterification, using sulfuric acid.

115a. S. M. Weisberg and E. G. Stimpson, U. S. 2,290,926.

116. R. J. Williams, A. Gabriel, and R. C. Andrews, The Relation Between the Hydrolysis Equilibrium Constant of Esters and the Strengths of the Corresponding Acids: J. Am. Chem. Soc. 50, 1267-71 (1928) C. A. 22, 2703 (1928). The ethyl esters of formic acetic, propionic, glycolic, lactic and of halogen acids were hydrolyzed directly until equilibrium was

reached. In general, when the esters of similar acids are compared, those formed from the stronger acids are more nearly completely hydrolyzed.

117. J. Wislicenus, Studien zur Geschichte der Milchsäure und ihrer Homologen: Ann. 125, 41-70 (1864). Di-sodium lactate and its methylation with methyl iodide were studied.

When ethyl alcohol vapors were passed through lactic acid maintained at 170-180°, alcohol, water, ethyl lactate and some lactic acid distilled over. Treatment of ethyl lactate with acetyl chloride yielded ethyl acetoxypionate boiling at 176-7° (733mm.); d_{17} 1.0458. Ethyl acetoxypionate was decomposed by heating with 2 volumes of water at 150°. Several products, including acetoxypionic acid were obtained. Salts of acetoxypionic acid were prepared.

118. C. E. Wood, Rotatory Dispersion of Certain Derivatives of Hydroxy Acids: J. Soc. Chem. Ind. 46, 424-7T (1927); C.A. 22, 1572 (1928). The esters of l-lactic acid from methyl to nonyl show increased rotation with shorter wave length. Irregularities in the molecular rotations suggest that the ester grouping has a spiral form with six atoms in the spiral.
119. C. E. Wood, J. E. Such, and F. Scarf, Rotatory Dispersion of the Esters of Lactic Acid. I. Normal Esters: J. Chem. Soc. 123, 600-16 (1923); C.A. 17, 1952 (1923). The original article should be consulted for the large number of density and rotation values given for the methyl to n-nonyl esters. See reference 47 under Methyl Lactate.
120. C. E. Wood, J. E. Such, and F. Scarf, Rotatory Dispersion of the Esters of Lactic Acid. II. The Isomeric Butyl Esters: J. Chem. Soc. 1926, 1928-38; C.A. 20, 3445 (1926). Secondary butyl lactate was prepared from the alcohol and ethyl lactate. The original should be consulted for physical constants and other data.

Isobutyl 1-lactate: Dry zinc ammonium salt (25g.), 80cc. isobutyl alcohol and 10.8cc. concd H_2SO_4 were heated on a water bath for 6 hrs. After four fractional distillations 11g. (b_{13} 73.1°) of ester (38% yield) was obtained.

t-Butyl 1-lactate. Dry zinc ammonium 1-lactate (27g.), 25g. tert. butyl alcohol, and 17g. concd. H_2SO_4 were heated at 60-70° for 7 hrs. Additional alcohol (10g.) was added during the esterification. Yield of ester was 7 g. (22%), boiling at 46-7° (9mm.).

d-sec.-Butyl 1-lactate. "Preliminary investigations showed that the best method for preparing higher lactic esters when only small quantity of alcohol was available was by intermolecular change from ethyl 1-lactate." Ethyl 1-lactate (17g.), 7.5g. sec-butyl alcohol, and 0.1cc. concd. H_2SO_4 were kept at 90-100° for 6 hrs. After 4 fraction distilla-

tions, 7g. of the desired ester was obtained. Similar, 8g. of ethyl d-lactate, 8g. d-sec-butyl alcohol, and 0.1cc H_2SO_4 yielded 5g. of ester; 17g. ethyl l-lactate, 15g. sec-butyl alcohol, and 0.2cc. H_2SO_4 yield the ester in 50% yield.

121. A. Wurtz and C. Friedel, Untersuchungen uber die Milchsäure: Ann. 119, 369-75 (1860). Ethyl lactate was made by heating a mixture of lactic acid and ethanol in a tube at 170°C .; b. 753 156° ; d_0 1.0542. The potassium derivative and ethyl iodide ethyl ethoxypropionate.

N-ethyl lactamide (m.p. 48° , b. 260°) was prepared from ethyl amine; this amide was compared with its isomer, ethoxypropionamide.

Ethyl lactyl lactate (b. 235° ; d_0 1.134) was made by heating ethyl chloropropionate ("chlormilchsaureather") with potassium lactate.

Ethyl dilactyllactate (b. 270°) was prepared; on hydrolysis ethanol and lactic acid were obtained.

122. Nitrating Monohydric aliphatic alcohols. Joseph A. Wyler (to Trojan Powder Co.). U. S. 2,105,802, Jan. 18. Nitration of an alc. contg. less than 6 C atoms, such as in the production of MeNO_3 from MeOH , is effected in the presence of an alkyl ester of a monohydroxy aliphatic carboxylic acid such as Et. lactate which serves to render the nitration a safe procedure.

123. Wurtz, Ann. Chim. Phys. 59, 169.

124. Wurtz, Ann. Chim. Phys. 63, 102.

C. PREPARATION AND PROPERTIES OF N-PROPYL
AND ISO-PROPYL LACTATES

1. W. J. Bannister (to Commercial Solvents Corp.) Aliphatic esters of Carboxylic Acids: U. S. 2,029,694, February 4, 1936; C.A.30, 1807 (1936); cf.C.A.29, 6902

Methyl, ethyl, and butyl lactates are prepared from the alcohols and lactic acid by introducing the alcohol into the acid at temperatures ranging from the boiling point of the formed ester to approximately 20° below said boiling point and removing the resulting vapors of the formed ester, water, and excess alcohol.

2. Charles Bogin (to Commercial Solvents Corp.) Use of Lactic Acid Esters in Nitrocellulose Brushing Lacquers: U. S. 1927, 539, September 19, 1933; C.A.27 5995 (1933).

Propyl, butyl, or amyl lactates are recommended.

3. O. Burkard and L. Kahovec, Raman Effect LXXXII. Nitrogen Compounds. 10. (Alpha-ammino and Alpha-hydroxy-propionic Acids and their Esters: Monatsh.71 333-45 (1938); C.A. 32, 8270 (1938)

Raman spectra of lactic acid and its methyl, ethyl, isopropyl, and butyl esters are recorded. Raman spectra for the corresponding alpha-methoxypropionates are included.

Isopropyl lactate (b.p. 158.6° to 161° at 760 mm) was prepared by heating lactyllactic acid ("Lactylmilch-saure") and isopropyl alcohol at 160-170° in a sealed tube for 4 hours.

4. H. V. Claborn and L. T. Smith. The Acetylation of Lactic Esters by Ketene: J. Am. Chem. Soc. 61, 2727-8 (1939)

The acetylation of ethyl and other lactates was studied.

5. J. W. E. Glattfeld and D. Macmillan. Lactones in Liquid Ammonia: J. Am. Chem. Soc. 58, 898-901 (1936)

Methyl, ethyl, propyl, and butyl lactates were ammonolyzed by liquid ammonia.

6. Goudet, These (University of Geneva, 1897)

The propyl, butyl, and isobutyl esters were prepared from the barium salt (according to Wassmer & Guye, J. Chem. Phys. 1, p. 278 (1903)

7. F. A. McDermott, Isopropyl lactate: Org. Syntheses 10, 88-9 (1930).

Isopropyl lactate was prepared in 60-68% yield from 450 g. isopropyl alcohol, 212g. of 85% lactic acid, 1 l. benzene and 5cc. concd. sulfuric acid. Isopropyl lactate had been prepared previously by heating lactic acid and isopropyl alcohol in a sealed tube at 170° (Silva, Bull. Soc. Chem. (2) 17, 97 (1872)), and from silver lactate and isopropyl iodide (Purdie and Lander, J. Chem. Soc. 73, 298 (1898)). According to McDermott, "direct esterification of acid with the alcohol, with sulfuric acid, has failed to give a yield greater than 20% of the theoretical amount, and the product has been less pure." McDermott emphasized the necessity of neutralizing prior to distillation. The product distilled at 75-80° at 32 mm. and at 166-8° under atmospheric pressure; some decomposition occurred at atmospheric pressure.

8. L. T. Smith and H. V. Claborn, Lactic Ester. Preparation and Properties: Ind. Eng. Chem. 32, 692-4 (1940).

Detailed directions are given for preparing methyl lactate and other esters from calcium and sodium zinc lactate in high yields. Sulfuric acid is used to neutralize calcium lactate. The original article should be consulted for details and physical constants of many lactic esters.

9. T. Purdie and G. D. Lander. Optically Active Alkylpropionic Acids: J. Chem. Soc. 73, 862-878 (1898).

Using Schreiner's method (Ann. 197, 13 (1897)), 240 g. (approx. 50%) ethyl ethoxypropionate was obtained from 500 g. ethyl bromopropionate. The cause of the low yield was attributed to the formation of ethyl acrylate. Methyl methoxypropionate (186 g. or 53% yield) was made from methyl bromopropionate (500 g.).

Propyl bromopropionate (200 g.) was added gradually to a hot solution of 26 g. sodium in 400 g. propyl alcohol. Heated for 1 hour, and then treated with CO₂. Yield was 55%; b.p. 187-8°.

10. T. Purdie and G. D. Lander. The Action of Alkyl Iodides on Silver Malate and on Silver Lactate: J. Chem. Soc. 73, 287-301 (1898).

From 173 g. silver lactate and 290 g. ethyl iodide was obtained 57 g. ester (55% yield) boiling at 151-4°.

From 235 g. silver lactate and 358 g. isopropyl iodide was obtained 40g. (25%) isopropyl lactate and some isopropyl isopropoxypropionate.

11. Silva. Bull. Soc. Chem. (2) 17, 97 (1872).

Isopropyl lactate was prepared by heating isopropyl alcohol and lactic acid in a sealed tube at 170. Isopropyl lactate is soluble in water. Isopropyl isopropoxypropionate was prepared from isopropyl lactate, sodium, and isopropyl iodide; this ester is water insoluble.

12. J. W. Walker. J. Chem. Soc. 67, 914-25 (1895). "The Ethereal Salts of the Optically Active Lactic, Chloropropionic and Bromopropionic Acids." The dry silver salt (45 g.) of d-lactic acid was added slowly to 66 g. of Methyl iodide. Reaction was vigorous. The mixture was finally heated a short time on the water bath. Distilled at 200 mm., 12 g. passed over at 105.5-106°. In a similar manner, 90 g. silver salt of l-acid and 150 g. ethyl iodide yielded 29 g. ethyl l-lactate, boiling at 67-64° at 25-22 mm.

Silver salt of d-acid (25 g.) and 38 g. propyl iodide yield 6 g. of propyl lactate, b_{15}° 122-3°C.

13. Eugene Wassmer and P. A. Guye, Recherches Physiocochimiques sur les ethers Actifs Lactiques et Maliques: J. Chim. Phys. 1, 257-288 (1903).

Before preparing active lactates, the preparation of inactive lactates was studied. It was found necessary to operate in absence of humid conditions because of the facile saponification of the esters.

Propyl ester: 8 to 10 g. zinc ammonium lactate and 20-25 cc. propyl alcohol mixture was saturated with dry HCL (6-8 hrs.), with cooling. After standing overnight, the zinc chloride was filtered, and the filtrate was distilled at 10 to 12 mm. After 2 fractionations there was recovered 0.2 cc. at 55-61°; 2 cc. at 61-2°; and 0.3 cc. at 64-70°. Other results are given below. The isobutyl lactate (3cc.) was treated with 15 g. acetyl chloride, heated for about 6 hours, and distilled in vacuo; 2 cc. of ester at 89.8 to 91° (see below).

Lactic acid derivative	: Alcohol or acid chloride	: B.P.: ° C.	: mm. Press.:	: Sp. gr.	: N_D	: Yield	: Fractionations
8 g. of l-	: 25 cc. propyl	: 60-1	: 10-11	: 0.957(54.8)	: 1.4182(17°)	: 1.5-2cc.	: 3
	:	:	:	: 0.994(17°)	:	:	:
8 g. of d-	: 25 cc. propyl	: 61-3	: 11-12	: 0.994(18°)	: 1.4194(15)	: Ca. 2cc.	: —
	:	:	:	: 0.957(54.8)	: 1.4186(16.8)	:	:
10 g. of d-	: 25 cc. N-butyl	: 70.5	: 10-11	: .985(16.2)	: 1.4232(16)	: 1.5-2cc.	: —
	:	: 73	:	: .942(59)	: 1.4230(17)	:	:
45 g. of l-	: 100 cc. iso-butyl	: 72-5	: 13	: .976(18)	: 1.4222(14)	: 16cc	: 6
	:	:	:	: .939(55)	: 1.4199(17.8)	:	:
11 g. of l-	: 20 cc. Heptyl	: 115-6	: 10	: .946(17)	: 1.4344(16)	: 4cc	: —
	:	:	:	: .912(57)	: 1.4317(21)	:	:
10 g. of l-	: 20 cc. octyl	: 126-8	: 11	: 0.938(17.8)	: 1.4393(13.6)	: 3-3.5cc	:
	:	:	:	: 0.905(56)	: 1.4376(16.8)	:	:
3 cc. isobutyl-1-lactate	: 15 cc. acetyl chloride	: 90-91	: 12	: 1.003(18)	: 1.4169(14.2)	: 2cc.	:
	:	:	:	: 0.958(61)	: 1.4140(20)	:	:
3 cc. isobutyl-1-lactate	: 15 cc. propionyl chloride	: 97.5-	: 11	: 0.988(17.5)	: 1.4207(15)	: Ca. 2cc.	:
	:	: 100	:	: .946(59)	: 1.4187(18)	:	:
3.5 cc. isobutyl-1-lactate	: 15 cc. butyryl chloride	: 110-	: 12-13	: .979(17.5)	: 1.4223(14.2)	: Ca. 2.5 cc.	:
	:	: 112	:	: .937(59)	: 1.4198(18.8)	:	:
4 cc. isobutyl-1-lactate	: 15 cc. benzoyl chloride	: 163-4	: 11	: 1.067(17.5)	: 1.4919(14.2)	: Ca. 3cc.	:
	:	:	:	: 1.032(57)	: 1.4898(18.5)	:	:

- 14 C. E. Wood. Rotatory Dispersion of Certain Derivatives of Hydroxy Acids: J. Soc. Chem. Ind. 46, 424-7T (1927); CA 22, 1572 (1928).

The esters of l-lactic acid from methyl to nonyl show increased rotation with shorter wave length. Irregularities in the molecular rotations suggest that the ester grouping has a spiral form with six atoms in the spiral.

- 15 C. E. Wood and J. E. Such and F. Scarf. Rotatory Dispersion of the Esters of Lactic Acid. I. Normal Esters: J. Chem. Soc. 123, 600-16 (1923); C.A. 17, 1952 (1923).

The original article should be consulted for the large number of density and rotation values given for the methyl to n-nonyl esters. See reference 47 under Methyl Lactate.

D. THE PREPARATION AND PROPERTIES OF BUTYL LACTATE

1. M. E. Bailey and H. B. Hass, New Methods for Resolution of Enantiomorphs. I. Rectification: J. Am. Chem. Soc. 63, 1969-70 (1941).

z-Methyl butyl 2-methylbutyrate.-- A mixture of 60 ml. of dl-2-methylbutanoic acid, 65 ml. of d-2-methyl-1-butanol, 100 ml. benzene and 1 ml. sulfuric acid were distilled (benzene returned) until theoretical amount of water had been removed. Optical isomers obtained by distillation through Lecky column (60 plates).

Butyl lactate. -- dl-2-butanol was esterified as described above with commercial grade of lactic acid which was 60 percent l and 40 percent d.

Butyl acetoxypropionate. -- Secondary butyl lactate was acetylated with acetyl chloride. B.p. 90-92° at 18 mm. d_{20} 0.9883 g/ml.

Butyl propionyloxypropionate. -- Sec.-butyl lactate was treated with propionyl chloride.

Amyl lactate. -- dl-2-pentanol and lactic acid yielded the ester, b.p. 75-8° at 10 mm., d_{20} 0.9615 g./ml.

Butyl propionoxypropionate. -- d-lactic acid, produced by fermenting whey with streptococcus lactus, was esterified with dl-2-butanol. The product was treated with propionyl chloride; b.p. 110-111° at 25 mm.

2. S. L. Bass and H. N. Fenn (to Commercial Solvents Corp.) sec. Butyl Lactate: U. S. 1956,972, May 1, 1934; CA 28, 4072 (1934).

Secondary butyl lactate (b. 172°, d_{40}^{20} 0.972) is obtained by heating anhydrous lactic acid and the alcohol to 170-175° in a bomb under pressure for four hours, and fractionating.

3. N. V. de Bataafsche Petroleum Maatschappij. Fr. 844,998, Aug. 7, 1939. The drain channels toward the wells obstructed by org. deposits and water can be effectively washed by using as washing liquid heterocyclic bases of the pyridine or quinoline type, their homologs and derivs. such a picolines, lutidines, alpha-colloidines, pyridinecarboxylic acids, pyridine-sulfonic acids, hydroxypyridines, amino- and diamino-pyridine, piperidine, quinolinecarboxylic acids, hydroxy-quinoline and generally all the bases contg. N obtained from coal tar and petroleum-cracking products. The bases are used alone or together with appropriate solvents such as methyl ethyl ketone, methyl propyl ketone, diethyl ketone, MeOH, iso-PROH, sec-BuOH, dioxane, tetramethylene oxide, furan, the Et ether or ethylene glycol, Bu lactate, glycol diacetate, the acetates of carbitol, benzene and acetone.
4. W. J. Bannister (to Commercial Solvents Corp.) Aliphatic esters of Carboxylic Acids: U. S. 2,029,694, Feb. 4, 1936; CA 30, 1807 (1936); cf. CA 29, 6902.

Methyl, ethyl and butyl lactates are prepared from the alcohols and lactic acid by introducing the alcohol into the acid at temperatures ranging from the boiling point of the formed ester to approximately 20° below said boiling point and removing the resulting vapors of the formed ester, water and excess alcohol.

5. Charles Begin, (to Commercial Solvents Corp.) Use of Lactic Acid Esters in Nitrocellulose Brushing Lacquers: U. S. 1927,539, Sept. 19, 1933; CA 27, 5995 (1933). Propyl, butyl or amyl lactate are recommended.
6. E. Bowden and H. Adkins, Hydrogenation of Optically Active Compounds Over Nickel and Copper-Chromium Oxide; J. Am. Chem. Soc. 56, 689-91 (1934) CA 28, 2699 (1934). Propylene glycol was obtained from butyl lactate.
7. O. Burkard and L. Kahovec, Raman Effect. LXXXII. Nitrogen Compounds. 10. (Alpha-Amino and alpha-hydroxypropionic Acids and Their Esters: Monatsh. 71, 333-45 (1938); CA 32, 8270 (1938).

Raman spectra of lactic acid and its methyl, ethyl, isopropyl and butyl esters are recorded. Raman spectra for the corresponding alpha-methoxypropionates are included.

Isopropyl lactate (b.p. 158.6° to 161° at 760 mm.) was prepared by heating lactic acid ("Lactylmilch-saure") and isopropyl alcohol at 160-170° in a sealed tube for 4 hours.

8. C. E. Burke and R. L. Kramer, Normal Butyl Nitrolactate; U. S. 1,598,474, Aug. 31, 1926; CA 20, 3460 (1926); Carbobutoxyethyl nitrate is prepared by nitrating butyl lactate. It is suitable for colloiding nitrocellulose as are also the similar amyl, hexyl and cyclohexyl nitrolactates.
9. R. Burns, D. T. Jones and P. D. Ritchie, Studies in Pyrolysis. I. The Pyrolysis of Derivatives of Acetoxypropionic Acid, and Related Substances: J. Chem. Soc. 1935, 400-6. The preparation and pyrolysis of ethyl acetoxypropionate was described, together with similar experiments.
10. E. R. Bush, Wood Stain and Filler Compositions: U. S. 2,161,503, June 6, 1939 (to Chadeloid Chemical Co.) CA 33, 7604 (1939). Lactic ester such as butyl lactate is used as lubricity agent.
11. T. F. Carruthers and C. M. Blair, (Carbide & Carbon) U. S. 2260,295, Oct. 28, 1941, CA 36, 854 (1942). The maleic diester of butyl lactate was prepared.
12. H. V. Claborn and L. T. Smith. The Acetylation of Lactic Esters by Ketene: J. Am. Chem. Soc. 61, 2727-8 (1939). The acetylation of ethyl and other lactates was studied.
13. "Liquid-Liquid Extraction Data (Correction)", Ind. & Eng. Chem. 33, 12, Dec. 1941, p. 1513.

14. C. L. Gabriel and C. Bogin, Normal Butyl Lactate: U. S. 1668,806, May 8, 1928; CA 22, 2172 (1928). This ester is prepared by heating butanol with lactic acid and distilling. It is a colorless, nearly odorless liquid boiling at 186-9° C.
15. O. Gerhardt, Butyl and Amyl Lactates as Solvents for Cellulose Lacquers: Chem. Ztg. 55, 222 (1931), CA 25, 3182 (1931).

A brief discussion of the properties that characterize butyl and amyl lactates as desirable cellulose solvents.

16. J. W. E. Glattfeld and D. Macmillan. Lactones in Liquid Ammonia: J. Am. Chem. Soc. 58, 898-901 (1936). Methyl, ethyl, propyl and butyl lactates were ammonolyzed by liquid ammonia.
17. Goudet, These (University of Geneva, 1897). The propyl, butyl, and isobutyl esters were prepared from the barium salt (according to Wassmer and Guye) J. Chim. Phys. 1, p. 278 (1903).
18. E. S. Greigor. Use of Lactates as Solvents: Peintures, pigments vernis 16, 141-3 (1939), CA 34, 4289 (1940). The ethyl, butyl and amyl esters of lactic acid have excellent solvent power for nitro-cellulose, cellulose acetate and various varnish resins and are useful in formulating lacquers, which may contain drying oils.
19. W. R. H. Hurtley and T. S. Wheeler, Lactic Esters: Brit. 346,486, Jan. 25, 1930; CA 26, 1940 (1932). Butyl lactate is prepared from ethyl lactate and butanol in the presence of strong acid.
20. Paul Kummel. Lactic acid esters. Farbe u. Lack 1938, 449-50. Com. Et and Bu esters of lactic acid were tested for stability by boiling for a short time with water and by standing in contact with water for 2 months. The amt. of acid formed was not excessive, the stability being about equal to that of AmOAc and superior to that of BuOAc. The Et, Bu and Am esters of lactic acid did not cause livering with zinc white nor discoloration with a Cu bronze. (See Paint, Oil and Chemical Review 102, 26 (1940). CA 33:4, p. 1523, 1939.
21. H. Martin and E. S. Salmon. The Fungicidal Proportion of Certain Spray-fluids, XI. Synthetic Solvents: J. Agr. Sci. 24, 469-90 (1934); CA 28, 6515 (1934); cf. CA 27, 3770. Ethyl and butyl lactates were studied.
22. N. Menshutkin. On the Esterification of Hydroxy Acids: Ber. 15, 162-5 (1882). Glycolic, lactic, and hydroxyisobutyric acids were compared by means of the following reactions: (1) Esterification with isobutyl alcohol, (2) Esterification with acetic acid, and (3) Auto-esterification or condensation polymerization. Rate and equilibrium data are given below:

	Rate	Equilibrium - "Grense" Limit
Esterification with isobutyl alcohol:		
Glycolic acid	-	67.67
Lactic acid	-	68.01
Hydroxyisobutyric acid	40.56	64.61

	Rate	Equilibrium - "Grense" Limit
Acetylation with acetic acid:		
Glycolic acid	-	49.22
Lactic acid	-	56.48
Hydroxyisobutyric acid	2.49	12.06
Auto-esterification:		
Glycolic acid	-	32.40
Lactic acid	-	32.16
Hydroxyisobutyric acid	2.61	10.83

23. P. D. Ritchie, D. T. Jones, and R. Burns. Improvements in or relating to the manufacture of derivatives of unsaturated acids: Brit. 424,885, Mar. 4, 1935.

Acyl derivatives of alkyl lactates were prepared and pyrolyzed; products were acrylic esters.

24. L. T. Smith and H. V. Claborn. Lactic Esters. Preparation and Properties: Ind. Eng. Chem. 32, 692-4 (1940). Detailed directions are given for preparing methyl lactate and other esters from calcium and sodium zinc lactate in high yields. Sulfuric acid is used to neutralize calcium lactate. The original article should be consulted for details and physical constants of many lactic esters.
25. Soc. Anon. des. Distil. des Deux-Sevres, Esters: Fr. 711,175, May 16, 1932; CA 26, 1616 (1932). Lactic acid is extracted from dilute solutions with butanol, and the extract is esterified to obtain butyl lactate.
26. E. A. Sym and W. Swiatkowska, Enzymic Esters Synthesis: Enzymologia 2, 79-80 (1937) (In German). CA 31, 5820 (1937); cf CA 30, 7601.

By the action of deacidified acetone-dried pancreas preparations in non-aqueous systems the following acids were esterified with butanol: malonic, succinic, phthalic, lactic, and salicylic.

27. Eugene Wassmer and P. A. Guye, Recberches Physicochimiques sur les ethers actifs Lactiques at Maliques: J. Chim. Phys. 1, 257-288 (1903).

Before preparing active lactates, the preparation of inactive lactates was studied. It was found necessary to operate in absence of humid conditions because of the facile saponification of the esters. For details, see reference 13 under Propyl Lactate.

28. C. E. Wood. Rotatory Dispersion of Certain Derivatives of Hydroxy Acids: J. Soc. Chem. Ind. 46, 424-7T (1927); CA 22, 1572 (1928).

The esters of l-lactic acid from methyl to nonyl show increased rotation with shorter wave length. Irregularities in the molecular rotations suggest that the ester grouping has a spiral form with six atoms in the spiral.

29. C. E. Wood, J. E. Such, and F. Scarf. Rotatory Dispersion of the Esters of Lactic Acid. I. Normal Esters: J. Chem. Soc. 123, 600-16 (1923); CA 17, 1952 (1923).

The original article should be consulted for the large number of density and rotation values given for the methyl to n-nonyl esters. See reference 47 under Methyl Lactate.

30. C. E. Wood, J. E. Such and F. Scarf, Rotatory Dispersion of the Esters of Lactic Acid. II. The Isomeric Butyl Esters: J. Chem. Soc. 1926, 1928-38; CA 20, 3445 (1926). Secondary butyl lactate was prepared from the alcohol and ethyl lactate. The original should be consulted for physical constants and other data.

Isobutyl 1-lactate. -- Dry zinc ammonium salt (25 g.), 80 cc. isobutyl alcohol and 10.8 cc. concentrated H_2SO_4 were heated on a water bath for 6 hours. After four fractional distillations 11 g. ($b_{13} 73.1^\circ$) of ester (38% yield) was obtained.

t-Butyl 1-lactate. -- Dry zinc ammonium 1-lactate (27 g.), 25 g. tert. butyl alcohol, and 17 g. concentrated H_2SO_4 were heated at 60-70° for 7 hours. Additional alcohol (10 g.) was added during the esterification. Yield of ester was 7 g. (22%) boiling at 46-7° (9 mm.).

d-sec.-Butyl 1-lactate. -- "Preliminary investigations showed that the best method for preparing higher lactic esters when only small quantity of alcohol was available was by intermolecular change from ethyl 1-lactate." Ethyl 1-lactate (17 g.) 7.5 g. sec-butyl alcohol, and 0.1 cc. concentrated H_2SO_4 were kept at 90-100° for 6 hours. After 4 fraction distillations, 7 g. of the desired ester was obtained.

Similar, 8 g. of ethyl d-lactate, 8 g. d-sec-butyl alcohol, and 0.1 cc. H_2SO_4 yielded 5 g. of ester; 17 g. ethyl 1-lactate, 15 g. sec-butyl alcohol, and 0.2 cc. H_2SO_4 yield the ester in 50% yield.

31. Joseph A. Wyler (to Trojan Powder Co.) U. S. 2,094,693, Oct. 5, _____. Nitration of materials such as sucrose or methyl glucoside is effected in the presence of a nitrated alkyl ester of a satd. hydroxy aliphatic carboxylic acid, containing not more than 2 carboxyl groups, such as nitrated Bu lactate which facilitates purification of the product, e. g. by use of EtOH.

